THE PRACTITIONER'S ENCYCLOPÆDIA

OF

MEDICAL TREATMENT

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THE PRACTITIONER'S ENCYCLOPÆDIA OF MEDICAL TREATMENT

PART I: METHODS OF TREATMENT
PART II: AGENTS IN TREATMENT

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WITH AN INTRODUCTION BY

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DEDICATED TO

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REGIUS PROFESSOR OF PHYSIC IN THE

UNIVERSITY OF OXFORD

AND TO

SIR THOMAS CLIFFORD ALLBUTT, K.C.B, M.D., F.R.S.,

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IN GRATEFUL REMEMBRANCE OF MUCH KINDNESS

EXTENDED OVER MANY YEARS

PREFACE

It is impossible to overrate the importance of Treatment in the Practitioner's art, and it has appeared to us that, despite the many excellent works on Treatment that have already appeared, there is still need for a *Practitioner's Encyclopædia of Medical Treatment* on the lines adopted by the contributors to this work.

It has been our endeavour to produce a compact single volume for the Practitioner, up-to-date and not of inordinate size or cost, written throughout by men of wide understanding and experience.

We have divided the work into two parts : (1) Methods of Treatment ; (2) Agents in Treatment. In the first part, certain general forms of treatment are dealt with and then the treatment for the various disorders is arranged in a systematic manner. We have excluded details of surgical operative measures and have dealt only with the indications for such measures and the general principles of the treatment of surgical cases and of acute surgical conditions.

In the second part will be found particulars of the action and use of different drugs, which are arranged in classes. This part of the work is not in any sense a catalogue of drugs or a list of prescriptions, but rather a guide to the practitioner for the principles and methods of medical treatment.

The opinions expressed as to the value of various drugs are in every case the result of the personal experience of the writer of the article only.

We desire to express our grateful thanks to Sir Thomas Clifford Allbutt, Regius Professor of Physic in the University of Cambridge, our master and friend for many years, for the Introduction to the work. To Dr. W. J. Dilling we are indebted for assistance in the preparation of Part II.

1915

W. LANGDON BROWN.
J. KEOGH MURPHY.

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INTRODUCTION

If for a moment we cast a glance backwards over the fields of the history of Medicine we shall see that Therapeutics has been fed from three main streams; not flowing in several beds, but, for much of their course at any rate, confluent. These three streams may for the present be signified as the Physical, the Empirical, and the Magical. The Physical may perhaps be called also the Rational method. Its doctrines and practice were developed in the great Hippocratic and Alexandrian Schools, and consisted in the study and application to disease of those mechanical and physical conditions on which normal health depends. It was largely, but not wholly, an especial direction and modification of the principles of hygiene, such as the influences of "Airs, Waters, and Places"; of exercises, active and passive, of dietetics, and so forth. In such a therapeutical system, a system of natural forces and conditions, flourished, as we should anticipate, a great, nay for that time a marvellous, school of Surgery.

But at no period was Therapeutics wholly independent of Empiricism. Early in his time Man discovered that certain substances entering into the body were so soon or even so instantly mischievous that the link of cause and effect was manifest even to a humble intelligence. Animals indeed have no little knowledge, by instinct as we say, what to take and what to avoid; a blind but not ineffectual empiricism. Thus Man learnt that not only in hostile but also in quiet things lay hid powers of evil; and if of evil why not likewise of good? Thus for good and evil, as weapons against his enemies, or as succour for himself and his tribe, Man laid the foundations of an empirical Medicine, such as ultimately we find, for the vegetable world, in Dioscorides. And out of empirical Medicine arose botany and zoology. The third or magical method of Therapeutics, very largely though not wholly of Oriental origin, consisted not in the natural (το φυσικὸν) but in supernatural or præternatural methods; in the aid of divine or demonic beings or occult influences. In European (Mediterranean) civilisation magical or mystical Medicine may be traced to the School of Pythagoras and the Sicilians, though their doctrines were soon swollen, and even overwhelmed, by grosser superstitions of Egyptian and Asiatic lore.

And so, with the temper and tides of nations and of cultures, have these three streams contributed, and do still contribute, to the practice of Medicine. If a few centuries ago the medicinal herb was to be culled only under astrological rules, if the healing waters lost their virtue until the angel stepped again into the well, so to-day herb or water is administered with the sauce of "suggestion." We refine our superstitions before we dismiss them. Thus, partly in an undisciplined empiricism, partly under the influence of magic, or magical suggestion, has grown up the monstrous pile of drugs, mineral, animal and vegetable, under which physician and pharmaceutist are groaning even to-day.

Once, for my sins, I was persuaded to join myself to a somewhat large Committee of the College of Physicians for consideration of the Pharmacopœia; or was it a general meeting *ad hoc* of the Fellows? I forget, and it matters not. Some of us were in favour of a drastic purgation, of a still further reduction of the mass, if not to the Wilksian "half dozen," at any rate to some handy and select circumscription. But no: no sooner did one of us conspirators lay hands upon a half-forgotten outlier of the collection than up sprang some colleague, or more than one, to declare that the defalcation of this substance would be to deprive him of one of the most precious of his remedial means. And so we proceeded, or so we stood still. I remember one of us, I trust not I myself, while speaking quite respectfully of "stomachic tonics," yet demurred to the multitude of this category, the number of vegetable bitters of which a smaller number might surely suffice. At length a daring spirit, coming to grips with detail, proposed to eject the individual "Chiretta." Who, he was bold enough to ask, who on earth ever prescribed Chiretta? Or if such an one there be, let his curiosity be satisfied with Gentian or Calumba! But even Chiretta had her champion. Personally, I penitently admit, I had seldom, perhaps never, heard of Chiretta, but therein lay a part of my ignorance and indifference as a practitioner of medicine. So, I believe, in the end we

were content to do, what most Committees do, to express admirable general sentiments, and then refuse to touch any particular proposition of change.

Perhaps, deep down in our thoughts, still flowed something of the stream of magic. Gentian and Calumba grow on Jordan, Chiretta is perhaps of "Mesopotamia." The champion of Chiretta, like the rest of us each with his own Chiretta, went home no doubt to prescribe his specific for an interesting patient, who again at her tea-table passed round the new and mysterious prescription to her gossips, and impressed by its mystery found in it a potency not vouchsafed to a more vernacular root.

As we say of our appetites, that being human they cannot, or ought not to, be extinguished, but are to be sublimated into more spiritual gifts, so is it with magical medicine. The *shaman* in his horns and feathers, or the more dignified *hakim* of Scott's novels, the one with his bloody instruments, the other with his precious balm or magical powder, in a more conscious and analytical age is succeeded by Mrs. Eddy and the ministers of Emmanuel. The *shaman* and the *hakim* were as sincere as was Paré with his puppy fat, and more sincere than Dr. Honeyman of Harley Street; and who is to throw the first stone at any of them? Magic was never a mere imposture, it appealed and appeals to-day to a large function of human nature. As the officers of the Salvation Army tell us, coarse and elementary natures need coarse and elementary stimulants; but the appeal, the appeal to faith and hope, is the same. The call is to the emotions to fill the sails of the medical bark; without a fair wind the prettiest medical craft may make slow way or none. Magical medicine springs therefore from a perennial source, and runs with the other currents; if, at times, like the Aar and the Rhone, the yellow and the sapphire streams run for many a mile without commingling.

Empirical medicine also has served us tolerably well; it is experiment, if not methodical experiment; without it we should have been poor indeed. For instance, our precious possession of the Jesuits' bark, or again, of colchicum, depended upon a therapeutical "shot"—a shot, one of a million, which hit the mark. The medicine was picked up, as gold has been picked up, by the navvy prospector innocent of geology; but the turn of the geologist follows, of him who tells men where the treasure may lie, and who finds it not by haphazard, but by a study of the structure of the earth.

And so we come back to the first stream—the stream of rational medicine, of remedies found by more and more searching analysis; but many a year will come and go before the scientific therapeutist becomes independent of the empiric. While the scientist is bringing thyroid extracts for myxœdema, or salvarsan for syphilis, the empiric brings iodide of potassium for the ray fungus, and the mystic enriches his formularies with Chiretta. Likewise it is said, but with less probability, that we shall always have to recognise "psychotherapy," the personal ascendancy and suggestiveness of the physician, with humbug as its inevitable shadow. Hope and faith, wisdom and purity are but incidentally the concern of the physician. At present we have to do with ill-educated patients: one man in illness is a great baby, another a dictatorial ass; the "suggestibility" of the patient is a legacy of the ignorance and pretension of the therapeutist, and of the unscientific state of the public mind; as therapeutics become more positive and the patient better instructed this wistfulness will vanish. No obsequious "tact," or "suggestion," is required nowadays to carry out an operation for appendicitis, because every silly lady thinks she knows all about it; some day the treatment of a pneumonia or of a gastric ulcer will be as intelligible and imperative, and stand in as little need of "psychological" garnish.

Among the many signs of promise in this bright morning of Medicine is our universal return, lay and medical, to that positive medicine of the great Greek period to which I have alluded. Even for the smart tea table the motley prescription is losing its "suggestiveness;" fine ladies who neglect their own children, are in a fuss about the babies of the poor, and we are all in a dilemma about the feeding of the children whose brains are under "education." The hygiene of life, inculcated by the chastening of the modern doctrines of tuberculosis—a chastening which has reached even the butcher and the milkman, of the care of the teeth, of the qualities of diet, of the training of the body, is the care of that preventive medicine which cannot be separated from therapeutics. The planning of cities and the material enfranchisement of the citizen are occupying the attention and, indeed, the drastic hand, of the statesman.

For the sick likewise physical methods are becoming every day more and more relied on. Baths of many kinds, methods and virtues, in England at first somewhat discredited by quackery and commercialism, are coming gradually, though as yet very imperfectly, under the immediate control of the expert physician. We are learning also the virtues of high altitudes, perhaps as stimulants of the bone marrow, of climates, and other natural conditions, as we are discovering more and more new resources in other physical means: in rest cures, passive and active exercises, respiratory gymnastics, electric and ray therapeutics, radio-activity, diathermy, and so forth. The principles

of diet, after some preliminary phases of eccentricity, are now better understood and applied; and under Pawlow's instruction the potency of flavours in diet—even, at a crisis, of fine wines—is comprehended. In Surgery, as in the early treatment of fractures and sprains, in the methods prescribed by Bier, and so forth, physical principles are coming to their own again, and achieving better and better results.

All this is fundamental; but we do not stop here: with surer and surer steps we are exploring the mazes of scientific therapy, in biophysics and in biochemistry; and if in the tangle of clinical phenomena a few chance gains may still be made by chance guesses, yet almost all progress worth reckoning is made more and more from the vantage ground of verified and measured chemical and physiological reactions. How far we are to make way on the more open plain of biophysics is a most fascinating "question." Difficult as its methods are, and fallacious save in the hands of highly skilled experts, yet, when thus exactly carried out, we obtain by them immortal knowledge. The mere mass mechanics of the living body count for much; and thence we penetrate into the secret ways of osmosis, of surface tensions, of ionisation and viscosity frictions restraining the travels of the ions, of adhesions and adsorption also—as seen, for instance, in Grünbaum and Coplan's remarkable asbestos experiments, of gas tensions, of blood pressures, and so on. We learn that some salts "ionise" in the body and some do not; some salts precipitate proteins, some do not; and we are detecting the part played by chloride of sodium in the body and the curious behaviour, positive and negative, of various quantities of calcium salts with the tissues and fluids.

And thus, before we enter upon Chemistry, we learn the true marvel of the cell wall, that wonderful little engine of concentration and inhibition, that centre of activity individual and social. If, as we shall see, much of its functions is to be interpreted by Chemistry, yet much also—as, for example, in the activity of the muscle cell—depends upon simpler physical laws, such as surface tensions. Many phases of the whole bodily system also, such as heat regulation in fevers, must in large part be explained on physical principles. Of inhibition again, of which as yet we know so little, is it metabolic (Gaskell), or is it physical; or not a uniform process, but a balance, a complex or variable function dependent upon place and time?

Thus by solubilities and insolubilities we pass into the domain of Chemistry; "organic" or "inorganic," I see no categorical distinction. Is it by physical law—osmotic or other tension, or by chemical law—solubility in lipoid and insolubility in water—that certain hypnotics, such as veronal or sulphonal, pass through the cell wall, while other cognate bodies are kept out? Is it by physical or by chemical hindrance that tetanus toxin does not reach the central nervous system by the blood stream, or that salvarsan cannot get at the spirochæta embedded in those parts? And, if we have marvelled at the cell wall, our marvel is increased when we contemplate the whole cell as a living being, a microcosm—a co-ordinated system of ferments, some of more general quality, many curiously specific; a system of co-operating phases, active, inhibitory and autolytic. If the balance be so shaken that autolysis prevails, as it may be studied in excised cells kept under living conditions, these lytic ferments escape and sap contiguous cells; and if in greater quantity spread destruction in the whole body (cachexia). These processes, with their illumination of disease, of splenic cachæmias perchance, we are seeing more and more clearly, and realising their meaning for the therapeutist, for him who searches to know how far the activity, if any, of his drug or other agent is a function of its chemical constitution, and how far its virtues are to be interpreted as a key fitting the biological lock (Fischer)?

Again we have to consider the effect of our agents not only in cells but also on cells, for ferments are not in the cells only; the blood abounds with them, diastatic ferments, protein splitters, and others, and is itself a sphere of chemical affinities and repulsions. Can any research be more "practical" than that of Lewis, Barcroft, Wolf and others on the distinction between cyanotic and acyanotic dyspnœa, and their explanation of this kind by falling alkalinity of the blood? If it be proved that every ferment is specific, whether for substances of external origin or for each and every substrate of the body itself, we shall have before us no doubt a vast and multitudinous scheme, but we shall pass out of the sphere of occult agencies into an open field of strategy.

No less liberating and refreshing is the discovery so lucidly and usefully set forth by Prof. Hopkins in his Presidential Address to the Physiological Section at Birmingham in 1913, that physiological and pharmacological discovery, when in its search for the processes of nutrition it was groping in bewilderment on the giddy levels of protein bodies of high molecular complexity, an attempt, in the words of Dr. Fielding Garrison, as baffling as an attempt to calculate the dynamics of will-o'-the-wisps, it was blindly thrusting itself into needless difficulties, was handicapping itself; and that in this research again we, not only may, but ought to, occupy ourselves with bodies of quite simple structure, such as the amino-acids. We may begin to build up our study of nutrition upon substances so simple as to be artificially synthesised. As

Prof. Hopkins put it, the significance of digestion is the very protection of the body from complexes, complexes foreign to itself. Its own structure it builds up with quite simple bricks. And, if we are to believe half what is told us about "vitamines," we are hindered, not by the complexity of such substances, but by their elusiveness, their infinitesimal and intangible proportions. So from all sides we are cheered on what has been a dreary way; our difficulties are not indeed fewer than we had supposed, but they are far more comprehensible.

We are learning, then, that if we are to make headway in the treatment of disease we shall not hunt in the dark for chance missiles, such as codein or uranium nitrate in diabetes. If by invisible means such a bullet be put into our hands we shall not despise it; strategically however we shall begin from the bottom, where there is more light, surer footing, and a way less intricate than we had supposed. We shall find that if many diseases are caused by alien invasion from without, others are due to individual default. In gout or diabetes a rung or two may have dropped out from the ladder of ascent and descent; or perhaps a rung was wanting from the beginning, but its defect, while the body was young, more easily compensated. Observers (Garrod and others) are now counting the rungs of these ladders and, in diabetes, are comparing glycosuria with glycæmia, are observing carbohydrate conversion in fever, are working upon the behaviour of fats and fat-splitting ferments, and testing these by processes as simple as surface tensions; a plan of work which, however refined and delicate, still lies within our understanding and our means.

And so with gout; does it matter if waste run in anions (meat) or kations (vegetables)? What is the chemistry of nucleoses and nucleosides, what the relation of amino-bases to hypoxanthins, etc.? In gout is uric acid in excess or only retained? What does colloid uric acid mean? If the uric acid is retained is this a renal fault? Is it, for example, an increased density of the glomerular membranes? Again, how far may waste be, or ought it to be, used up again? The purin bases have been brought well within the range of our methods, and we see the part they play in nuclein exchange; but so far we have not learned much more about them. Can we yet say how far and in what way, if in any way, they are injurious? With Fischer's help, we can begin by synthesising these bodies, follow up glycosides from uric acid, and speculate on the relation of purin glycosides to gout; but between these terms there is as yet, I fear, many a *hiatus valde deflendus*. In the reports of societies, we read columns of discussion, but little deposit of knowledge. Still now we see the road, and certain milestones; and pilgrims forging ahead.

A very subtle and pretty way of following up the trail of morbid processes is by the methods of staining, brilliantly developed by Ehrlich and ingeniously carried forwards as intra-vital staining by Goldmann, whose premature death deprived us of the full benefit of his researches. Not only by stains can we follow up, as it were, the scent of Nature's tracks into their secret haunts, but the structural constitution which adapts the stain to the natural process enables it so to enter into the action (Fischer's key and lock again), that by another turn of pharmacodynamic ingenuity a stain may neutralise it. Thus Ehrlich found in methylene blue some remedy for quartan fever, for bovine piroplasmosis in trypan red, and indicated some other remedies not as yet perhaps adequately investigated, while Nuttall found in trypanblue a remedy for piroplasmosis in dogs and other animals; however, these few points are but points in a large field of discovery, and have their application in the specific affinities of certain drugs for certain physiological tissues.

In the sphere of Immunity Behring's first exploits raised enthusiastic hopes of a triumph of therapeutics, hopes so far, unhappily, if not extinct very much sobered. Beyond diphtheria and typhoid fever we have gained little certain ground. The result of Sir A. Wright's campaign against pneumonia have yet to be appraised. At many points anaphylaxis baffles the investigator. Tolerance again may compel us, if we would exterminate a parasite, to try to do so, in Ehrlich's phrase, "at one blow," by a *therapia sterilisans magna*.

From such researches emerged the distinction between antitoxic and antibacterial defences, a cardinal distinction for the therapeutist. And as my purpose in this Chapter is to emphasise the way of discovery by simplification, I would call attention to certain of Sir A. Wright's experiments *in vitro* which, because they are in *vitro*, have in my opinion received less regard than they will prove to deserve. I refer to his experiments with ethylhydrocuprein on the pneumococcus (a method extended later by Ehrlich to streptococci). In like manner the comparison of the influence of various agents upon the conspicuous vivacity of trypanosomes in the field of the microscope should lead to valuable results.

Another direction of pharmacodynamic research may well prove to be along the line of immune body and ferment parallelism, if in this brief review I may be forgiven for a phrase so curt and arid.

None of us can touch on the dynamics of disease without a tribute to the magnificent—I can use no less a word for it—the daring and original theory of Ehrlich on what I will call the mechanism of specific affinities. This theory, if from so humble a service I may speak of myself,

has filled me, from the time I first heard of it, with admiration; I have wondered and wonder still, at a conception so far beyond any flights or any visions of my small imagination. It stands worthy of a place beside the serial and ring theory of chemical combination. So far from being a nebulous, or a fantastic idea, every day is proving its explanatory power; as for example in the derivation of the test of Wassermann. Ehrlich's conception will, I believe, take its place as the organon of pharmaco-dynamics. By its use, or at any rate by its inspiration, the therapeutist, working on the special affinities between drugs and tissues, will learn from Ehrlich how to add to the arsenal of the "charmed bullets which strike only the objects for whose destruction they were forged."

The brilliant discoveries in the field of what I may broadly call Tropical Medicine are not only lifting our eyes out of the vague to definite and comprehensible conceptions, but, moreover, our hands to such achievements as those of Ross in Egypt and of Gorgas in Panama.

Nor are these achievements confined to "bodily" disease: the new disposition to positive conceptions has become strikingly manifest in the sphere, hitherto so remote and metaphysical, of "Mental Disease." The secrets of Tabes and Dementia Paralytica are torn from "the lap of the gods"; it depends only on our determination when these horrible scourges shall be brought to extinction. And we shall not rest here; analogy hints to us that not these only but other such grievous adversities of the best part of man, such, let us guess, as Dementia præcox, may be, in like manner, results of tangible poisons to be detected and checkmated.

Of late years we have heard much, and justly, of great advances in Surgery. But Surgery is, of course, only one of the many methods of treating all or any disease. The division of Medicine into inner and outer, with its corresponding bisection of the physician, is a comparatively modern convention, a convention which arose in the Roman and medieval contempt of clerk for craftsman. Hippocrates, Erasistratus, or Galen would have laughed it to scorn. Surgery is either "medicine without diagnosis" or is virtually correlative with the whole field of practice. As for many outward maladies we may need neither knife nor splint, so of few inward can it be said that Surgery will find no place. A surgeon in large practice, making his daily autopsies, is better informed, let us say, on gallstones, gastric ulcer, peritonitis, obstruction of the bowels and so forth than the ablest of his "medical" colleagues. But even yet, I believe, cases of appendicitis or intussusception are, on a point of politeness, carried first to the "medical" wards. It is pathetic to see year by year the physician retiring from large departments of his own affairs in dumb submission to the dead hand of the medieval University of Paris—itself perhaps the most perverse of all the greater institutions of Europe. Some "specialising" there must be; the physician will concern himself with such practice as he finds himself best fitted by taste and skill; but his sphere once chosen, surely as a man of decision he should be regarded as free to use all and any ideas, all and any means of cure within his reach. The present custom puts both "physician" and "surgeon" in a false position, and limits their outlook on their world. The gynæcologists, partly no doubt to avoid multiplication of advisers in cases of secrecy, but chiefly perhaps because a few of them were men of decision, fought and won the battle of freedom for themselves; it is for their "medical" brethren to follow the example.

My friends, the Editors, invited me to write a Preface to this work. On a mountain in Switzerland, far away from books and papers, I have ventured to make this sketch of the new Therapeutics. The sketch, as a sketch, is faulty enough. When I come to read it over I find no allusion to Colloid Chemistry—but this is now, perhaps, a somewhat hackneyed subject; none to Hormones and the Chromaffin system, especially to adrenalin which does not disdain to put on a crystalline form; and so on for many a gap. At the risk of wearying the reader by my personal impressions, I have rambled at large among the discoveries which most have awakened my own enthusiasm, and banished to their own under-world the blind and formal drug-mongering of the elder tradition, and indeed of my own younger days, in the practice of physic. What a joy it would be to start from the present and, with these new visions, to begin it all over again!

T. C. A.

Part I

METHODS OF TREATMENT

GENERAL METHODS

THE DIETETIC FACTOR IN TREATMENT

In order to apply the dietetic factor in the treatment of disease, it is necessary to understand something of the methods of nutrition in the healthy man.

Quantity of Food required.—It is curious that physiologists have never been able to answer definitely the question, "How much ought we to eat?" More than forty years ago, Voit fell back on the instinctive appetite of the average man as his guide, and fixed the minimum protein requirement at 100–125 gm. a day. Atwater has recently come to much the same conclusion by comparison of the diets selected by a large number of individuals in varying conditions, the main difference being that for very hard work the protein was increased to 175 gm.

The following tables were prepared by Von Ranke, based on Voit's work. Table A is for a man not doing much muscular work; table B shows the modifications necessary for hard muscular work—

	A	B
Protein	100	125
Carbohydrate .	240	500
Fat	100	50

Diet B contains 300 gm. of carbon and 20 of nitrogen.

Translating this into the terms of ordinary foods, Waller has drawn up the following diet—

Foundation:	1 lb. bread.
	½ lb. lean meat.
	¼ lb. fat.
Accessories:	1 lb. potatoes.
	½ lb. milk.
	¼ lb. eggs.
	⅛ lb. cheese.

This contains about 330 gm. of carbon and 21 of nitrogen and is, therefore, somewhat richer than diet B. The average day's work requires 3000 calories of energy. Diet B contains 3027·5 calories and would, therefore, appear to be adequate in this respect also.

These conclusions have been seriously questioned by Chittenden, who, by observations continued for six months on himself, his assistants, a number of students and a squad of soldiers, showed that nitrogenous equilibrium could be maintained on about half this amount of protein with no diminution of physical or mental energy, but rather an increase.

In the following diet given by Chittenden, the total protein amounts to 41 gm.—

Breakfast.—Coffee, cream, milk and sugar.

Lunch.—Omelette, bacon (10 gm.), potato, butter, bread (or biscuit), fruit and sugar.

Dinner.—Beefsteak (34 gm.), or lamb chop (32 gm.), peas, mashed potatoes, bread, butter, salad, coffee and sugar.

Chittenden has certainly proved one point of great interest and importance: that the minimum protein requirements of the body are much less than was supposed, but he goes much further and maintains that the minimum is also the optimum. He really produces no evidence in favour of this view, however. He is, in fact, obsessed with the old idea that the body is unable to make any other use of protein food than to repair tissue waste—an idea which other lines of work have rendered improbable. The physiological minimum is not necessarily the physiological optimum.

Experience shows that where there are races taking a protein-rich diet and a protein-poor diet living side by side, the morbidity and mortality of an epidemic are higher in the latter. Again, the rapid rise of Japan corresponds to the adoption of a more liberal nitrogenous diet. To this Chittenden retorts that prosperity causes an individual or a race to elaborate the menu, and that increased food is not the cause of the improvement.

Protein Metabolism

The end products of metabolism of the different forms of protein, though conforming to a certain general type, differ widely in detail, yet the chemical constitution of the tissues remains the same whatever the form of the food protein. Thus, horse's blood is rich in tryptophan, one of the aromatic bodies, while wheat protein such as glidine is very poor in it; yet, if a horse be bled and then fed on pure glidine until it has regained its former weight, the amount of tryptophan in its blood is as great as ever. The change from food protein to tissue protein is much more profound than was formerly suspected.

When Kühne showed that at least a portion of protein is broken down by pancreatic digestion into leucin and tyrosin, the purpose of this apparent waste puzzled physiologists. For it was then believed that animals require their protein ready-made, and are incapable of the simplest steps towards its synthesis. But the discovery of erepsin in the secretion of the small intestine by Otto Cohnheim in 1903, proved that not only a part but the whole of the protein molecule ingested was thus broken down into amino-acids, and that dogs could live as well on a complete mixture of these end products as on ordinary protein.

The Building-up of Protein. — It has been well said that just as a Gothic cathedral cannot be built out of a classical temple without reducing it to its constituent stones, so the protein tissues cannot be built out of the protein food until it has been split up into its constituent groups. To continue the analogy, at the end of the rebuilding there must be many stones which will not fit, and so cannot be built up into the new structure. This explains the apparent waste of nitrogen on feeding a starving person with protein. A large proportion of the administered nitrogen appears in the urine, although the tissues might be thought to be clamouring for protein. But they can only utilise stones of the right shape, as it were; one cell may require arginin, another leucin, and so on. They cannot make use of an entire molecule of protein. The increased excretion of nitrogen represents the fragments that will not fit into the gaps. We begin to see then why protein is one of those things of which, as Hutchison says, it is necessary to have too much in order to have enough.

The wider the choice of protein fragments which the tissue cells are offered, the easier and more satisfactory the process of reconstruction. In this way we can understand the greater resisting power of the tissues to invasion by disease when protein has not been cut down to its irreducible minimum. The more the food resembles the flesh into which it has to be incorporated, the easier the metabolic task. This truth underlies Hopkins' humourous advocacy of cannibalism.

The end products of protein digestion are absorbed as such and pass by the portal vein to the liver. The liver has to select those groups required by the tissues and allow them to pass on, while the others undergo denitrification there. By oxidation and subsequent dehydration they can be converted into urea. But, since urea contains more nitrogen than carbon, and protein the reverse, there will be a considerable amount of carbon at the disposal of the body as a source of energy when this disintegrative process is complete.

Neither are the basic nitrogenous groups which have been split off entirely wasted. They are probably of service in preventing acidosis. It is much easier to produce acid intoxication in a fasting than in a well-fed animal. In carnivora, with their abundant protein diet, there is a marked power of protective ammonia formation, and the source of this ammonia is the NH_2 groups split off from the protein. The functions of protein food are, therefore, three: (1) to repair tissue waste; (2) to supply energy; and (3) to combat acidosis.

The Origin of Urea.—Folin's researches have shown that by far the greater part of the urea in urine comes from this nitrogenous excess, direct from the food, and has never formed part of the tissues. This has an important practical bearing on the value to be attached to estimations of urea. Many far-reaching conclusions have been drawn from such estimations in, for instance, uræmia or the toxæmias of pregnancy, but very little attention has been paid to the diet in such cases. It is obvious that a chronic nephritic who is taking very little nitrogenous food, or any one who is rejecting food by vomiting, necessarily excretes but little urea. For within very wide limits the amount of urea excreted depends on the amount of nitrogen ingested and on very little else.

The Economy of a Mixed Diet.—It may be urged that as protein contains fatty acid groups and generally carbohydrate groups as well, it is capable of sustaining life by itself. This is, to a certain extent true, but practically a purely protein diet is open to grave objections. The diet tables given above show that the body requires fifteen times as much carbon as nitrogen. In protein the carbon to nitrogen ratio is 3 to 1; so that, to obtain all the carbon required from protein would mean a great waste of nitrogen, since for every part of nitrogen utilised there would be four wasted. This would mean the digestion of an enormous amount of protein. It has been estimated that it would require $4\frac{1}{2}$ lb. of lean meat in the day to satisfy the bodily needs if this alone were taken. Such an amount would be almost impossible to digest and it would throw an entirely unnecessary task on the body in the formation of urea. The normal individual is only able, and that much against his will, to consume about $3\frac{1}{3}$ lb. of meat daily for at most three days. Hence the economy of a mixed diet, whereby the carbon required can be obtained from carbohydrate or fat without unnecessary nitrogen. It may be noted that the appetite instinctively selects a mixture of foodstuffs on the same plate and even in the same mouthful. The addition of potatoes to meat and of butter to bread and

cheese, are familiar examples of this. Another disadvantage of an excessive protein diet is that it entails the consumption of many aromatic and sulphur groups which are particularly prone to putrefactive changes by the action of intestinal bacteria.

Protein or its products are absolutely essential to tissue building. The great advantage of some excess of protein beyond the amount required for this, is that it provides energy of a high grade at short notice. A high proportion of the animal protein ingested can be utilised in this way. Gelatine may be looked upon as an imperfect protein in that it lacks the aromatic groups, and it is therefore incapable of entirely replacing ordinary protein in the diet. It is, however, a protein sparer like carbohydrate or fat, but it is so to a much higher degree because it can also supply some of the nitrogenous groups contained in protein. It might be urged that the absence of aromatic groups render it highly suitable in the treatment of intestinal intoxications. Unfortunately, it has only a limited sphere of usefulness here as a large amount of gelatine becomes intolerable to the taste.

Carbohydrate Metabolism

Carbohydrate forms the largest bulk of the diet, even allowing for the fact that, as usually eaten, a considerable amount is in the form of cellulose, which is not digested except by bacterial action and is, therefore, not utilised by the body. It is digested to a limited extent by the saliva if thoroughly masticated, and salivary digestion can proceed for a considerable time in the stomach until the contents become acid. The gastric juice has no further action on carbohydrates beyond hydrolysing starch to a certain extent as any other acid medium would do. It follows, then, that it is the harder, drier forms of carbohydrates which have the best chance of being digested by the saliva, yet, in the treatment of digestive disorders, nothing is commoner than the administration of large quantities of starch in a soft form. As Sir Clifford Allbutt says, "There is no superstition more tenacious of life than that which prescribes carbohydrates to all dyspeptics as 'so digestible,' and into weak stomachs, ready to dilate, is thrown a mass of such a dish as rice-pudding—a bulky food, imperfectly salivated and peculiarly apt to decompose with the disengagement of volumes of carbonic acid gas."

The Functions of Carbohydrates.—The digestion of carbohydrates is completed by the pancreatic juice and the succus entericus of the small intestine. After absorption, mainly as dextrose, one of four things may happen to it. It may be stored as glycogen; it may be stored as fat; it may be consumed at once for muscular energy, and, lastly, any excess over the amount which can be dealt with in these ways will appear as sugar in the urine.

1. **The Storage of Glycogen.**—This is a temporary but necessary expedient, since it is impossible for a large amount of a crystalloid-like sugar to remain free in the circulation; the liver may be looked upon as a carbohydrate bank whose stores can be drawn upon at short notice.

2. **Storage as Fat.**—Lawes and Gilbert showed by their classical experiments that the popular idea of carbohydrates being fattening foods is correct. By feeding pigs on barley-meal of known composition they were able to prove that too much fat had been laid on to have come from anything but carbohydrate.

3. **Carbohydrate and Muscular Energy.**—The earlier experiments on the relationship of carbohydrates to muscular energy failed to take into consideration the influence of diet on the source of muscular energy. On a mixed diet, increased work is not followed by a proportionally increased nitrogen output, but on a purely protein diet the increase of work and nitrogenous excretion run parallel. In other words, the body uses whatever foodstuff is most available as a source of energy. One simple consideration will prove that there is no essential difference between the metabolic process in rest and activity. The respiratory quotient is raised by increased consumption of carbohydrate and lowered by increased consumption of protein or fat. In exercise it is not altered, showing that although the body consumes more during exercise than in rest, it continues to use the various foodstuffs in the same portions.

Carbohydrate is an important source of energy because it constitutes so large a part of the food—75 per cent. of the total ordinary diet, but it has no specific virtue in this respect. In this matter there has long been a discrepancy between theory and practice. Abundance of protein food has been found by experience to constitute the best diet for training, which was difficult to understand as long as carbohydrate was believed to be the unique source of muscular energy. Now we know that protein can also act in this way while, in addition, it renews the machinery by increasing metabolic change and prevents the accumulation of fat. The machinery also appears to work more economically when protein is the principal fuel; there is less distress, dyspnœa and sweating.

In the article on *Diabetes* the objections to the total withdrawal of carbohydrates from the diet are discussed. Here it is sufficient to point out that of all the foodstuffs carbohydrates are the richest in oxygen and that in

their entire absence it is impossible for the oxidative changes in the body to be complete. Hence the production of abnormal acids instead of CO_2 and consequent acidosis. The consumption of as little as 30 gm. of sugar in the day will, however, prevent the occurrence of this acidosis.

Fat Metabolism

Turning next to the metabolism of fat in the body we may inquire first how far the different foodstuffs are responsible for its deposit.

1. **Fat as a Source of Fat.**—If more than a moderate amount of fat is given it is directly deposited. By various methods it has been shown that the fat of the food can directly influence the composition of the fat of the tissues and of the cream in milk.

2. **Carbohydrates as a Source of Fat.**—The proof of this has already been given. It is possible that carbohydrate is the main source of an animal's own fat, the fat of the food being either directly deposited as such or consumed at once. This would accord with the experience of those who have used Banting's method for reduction of obesity, that it is better to allow the patient a little fat than to allow him carbohydrate. In short, carbohydrate is more fattening than fat, probably because of the ease with which it can be assimilated in large amounts.

3. **Protein as a Source of Fat.**—We should not expect protein to be a fattening food, since it is difficult to satisfy the daily requirements of the body with this alone, and therefore still more difficult to acquire a surplus on it to be deposited as fat. That lower organisms can convert protein into fat is certain, but there is no evidence that mammals can effect this conversion, though proteins contain plenty of amino fatty acids. In phosphorus poisoning there is an accumulation of fat in the liver which was formerly believed to be due to degeneration of protein. But Rosenfeld showed that it was due to transference of fat from other parts of the body, for if abnormal fat had previously been given it was the abnormal fat which was found to have accumulated in the liver. The condition is one of fatty congestion. Certain other poisons such as chloroform and diphtheria toxin have a similar action. The normal reactions of the liver are retarded, probably by inhibition of the oxidases. Leathes has shown that one very important duty of the liver in metabolism is to receive the less active saturated fats from the body and to convert them into unsaturated fats which are more oxidisable, and, therefore, more active. Should the liver be unable to do this the tissues are starved of oxidisable fat, while the inactive fat accumulates in the liver. And the greater the "fat hunger" of the tissues, the more will they tend to precipitate fat on to the liver to be prepared for their use. We can understand, therefore, the extraordinary speed with which the liver becomes engorged with fat in such a condition as post-anæsthetic poisoning. But it is quite different from the protein giving rise to fat. In the so-called "fatty degeneration" of sepsis and profound anæmias there is often less fat than in a normal organ, but the degenerative process has set the fat free from its combinations, so that it is obvious to the naked eye or microscope instead of only being extracted by elaborate chemical processes.

Functions of Fat.—The chief value of fat, apart from its mechanically protective function, is its calorific value, amounting to 9·3 calories for each gm. consumed as against 4·1, the caloric value of each gm. of the other two foodstuffs. It is inferior to carbohydrate as a protein sparer, and the breaking down of the tissue protein is not decreased by giving fats to a starving animal or to any great extent in diabetes. Fats can also act as a source of energy though carbohydrates are usually drawn upon for this purpose first. The other main function of fat is to act as a reserve store which can be drawn upon at need.

For all practical purposes fat is only digested by the pancreas and absorbed with the aid of the bile. When fats break down they normally are completely oxidised into water and CO_2. If incompletely oxidised, however, as they are in such conditions as diabetes, mountain-sickness, bronchopneumonia, etc., they form oxybutyric acid which gives rise to diacetic acid and may ultimately decompose into acetone. (See articles on *Auto-intoxication* and *Diabetes*.)

Disadvantages of Fat.—Fat has distinct drawbacks in that it is expensive, and that it is relatively indigestible probably because it partially inhibits the secretion of gastric juice. It is usually disliked by children, who can obtain most of its advantages from carbohydrates, which they generally prefer. In view of its inhibitory effect on gastric secretion, it may be good moral discipline to force a child to eat fat, but it is bad physiology. In hot climates fat is disadvantageous from the amount of heat to which it gives rise, but in cold climates it would be difficult to take sufficient bulk of carbohydrates to supply the necessary heat. Moreover, in the coldest climates, fat is more easily obtained than carbohydrate. It is generally said that stout people feel the cold less and suffer more in heat. A moderate excess of fat in the tissues has the advantage of forming a reserve in the event of wasting diseases. The disadvantage of an excess is that the carrying about of extra

inert material consumes energy which might be better employed. It therefore follows that the obese are nearly always short of breath.

The rôle of each of the foodstuffs having been explained, it will be clear that the diet which contains all of them is a physiological ideal and that, while it is impossible to do without protein, it is also highly inadvisable to do without carbohydrate altogether. Probably the easiest foodstuff to do without altogether is fat, but the objections to this have been already explained.

Milk is often spoken of as a perfect food, meaning that it contains all the foodstuffs approximately in the right proportion, but it can only be considered a perfect food for the infant. The percentages of the foodstuffs required by a man doing hard muscular work and those contained in the solid part of the milk are shown in the following table—

	"Ideal"	*Human Milk*
Protein	18·5	20
Carbohydrate . .	74	50
Fat	7·5	30

It is also too dilute a food for adults, and this limits its usefulness in the treatment of such diseases as gastric ulcer and nephritis. As to inorganic constituents, it is deficient in iron and too rich in calcium, so that prolonged milk-feeding is apt to produce anæmia and tends to thrombosis.

The marked frequency of thrombosis following enteric fever during the South African war has been said to be due to the extensive use of condensed milk which is richer in calcium and poorer in citrates than ordinary milk. Milk has a feebly stimulating effect on gastric secretion; on entering the stomach it curdles, unless the gastric contents are already distinctly acid, in which case a precipitate of caseinogen occurs. Curdling was formerly considered an advantage in that it would prevent the escape of valuable nourishment from the alimentary tract too rapidly, but, as a matter of fact, the use of sodium citrate, which prevents curdling, has proved a great advantage in rendering milk more assimilable. This suggests that curdling has not any real advantage. Curdling is apparently the first stage in the activity of almost all proteolytic ferments, and is therefore more marked with the weaker ferments in the stomach than with the stronger ferments in the pancreas. If tryptic activity is delayed by the addition of six per cent. sodium chloride, curdling becomes much more marked. The conclusion, therefore, is that the formation of a curd, which has certain obvious drawbacks, has no real physiological advantage, and processes tending to prevent its occurrence may unhesitatingly be employed when digestion of milk is difficult. Ordinarily speaking, the addition of 1 gr. of citrate of soda to each ounce of milk will prevent the formation of a dense curd, and this has the further advantage of throwing some of the excess of calcium out of action.

Vitamines.—Lately it has been shown what an important part both in growth and disease is played by other constituents of ordinary foods besides the three main foodstuffs. These are not the saline ingredients but organic substances present in minute quantities and easily overlooked. Hopkins found that when food completely freed from them was given to young animals they entirely ceased to grow, though the normal amount of food was taken. If the material removed by alcoholic extraction were returned to the food, or if minute quantities of milk or fresh tissue extracts were added, the animals grew normally. This may have an important bearing on the dietetic treatment of malignant disease, as the rapid and disordered growth of a neoplasm demands more of these organic substances than ordinary tissues. (See article on *Non-Operative Treatment of Malignant Disease.*) Funk, who has added so much to our knowledge of this subject, found that chickens fed with red rice failed to grow; but that on the addition of some yeast or powdered sarcoma cells to the rice they grew, though not so much as on ordinary diet. Not only may growth be inhibited by the lack of these organic substances, but actual diseases may be induced, such as scurvy, infantile scurvy and beri-beri. According to some, epidemic dropsy and pellagra have a similar origin. Fresh milk contains both an anti-scorbutic principle and a substance inhibiting beri-beri. It is now well recognised that heating milk in an autoclave and sterilisation methods generally result in the loss of the anti-scorbutic principle. Hence infantile scurvy in children entirely brought up on such foods. Holst and Frölich induced in guinea-pigs a fatal disease resembling scurvy by feeding them on barley, oats or rye, and cured them by adding fresh potatoes, apples, carrots, cabbage or lime juice. These were useless in the dry form, and the expressed juice lost its activity if heated or kept long, except lime juice, which was not inactivated by boiling for an hour; the stability of its anti-scorbutic principle probably explains its great value in the days of long voyages without fresh food. To such substances Funk has given the name of *Vitamines*, and he believes he has isolated them in a crystalline form and found them to be basic in character. Thus to the beri-beri vitamine in the outer layer of rice he assigns the formula $C_{17}H_{20}N_2O_7$. He has also found it in milk, yeast, ox-brain and lime juice.

The experiments of Thompson and Caldwell point to the existence of similar substances in meat-extracts which play a part in accelerating growth. We may in consequence have to revise our estimate of the value of beef-tea. Its nutritive content is practically nil, and till now the most positive evidence of its stimulating action has been its exciting effect on gastric secretion. As Hutchison points out, the value of oatmeal in some cases of diabetes may be due to its containing a vitamine, while the old controversy as to the respective merits of white and whole-meal bread assumes a new aspect. Evidently a diet is not necessarily adequate because it is of sufficient caloric value and adequate protein content. "It is necessary that it should contain these unknown substances as well, which act more like drugs than foods, and which may play a specific part in metabolism. . . . The practical result of the knowledge already acquired should be to confirm our old belief in the value of a mixed diet, drawn from as many sources as possible, and also to discourage cranky and one-sided views and practices."

Salts in Metabolism.—That inorganic salts are also essential ingredients is generally agreed, though it must be admitted that many of the experiments relied upon to prove this are now invalidated, since the methods employed would also have removed vitamines. But that "salt action" enters definitely into the life of the cell is certain. The three essential metals are sodium, potassium and calcium, while magnesium and iron are presumably also necessary. (See article on *Salt Action.*) Excess of sodium chloride may cause œdema even in an apparently healthy person. Excess of calcium has been thought to increase a liability to thrombosis, but the liability must be already present. Deficiency of iron in the food can, apparently, induce anæmia. But the list of such influence of salts on disease is a short one. Although deficiency of phosphorus in the diet has been held responsible for vague ill-health and actual disease, there is no satisfactory proof of this.

Dietetic Restrictions.—It would perhaps be misleading to assert that the dietetic factor in the treatment of disease has been exaggerated, but it has certainly been misunderstood. There has been a tendency to regard the body too much in the light of a test tube into which reagents could be poured and a definite reaction produced. But the problem is much more complicated than that. Simple chemical explanations of disease have invariably broken down with increased knowledge. Thus it is now recognised that the albumen of the food cannot directly influence albuminuria, that retention of ingested purins is not the cause of gout, that the dietetic treatment of glycosuria is not comprised in abstention from starch and sugar, and that oxaluria and phosphaturia can still occur when oxalates and phosphates have been carefully eliminated from the food.

Sir William Roberts declared years ago of some dietetic restrictions: "They are for the most part quite unmeaning; they stand on no ground of science or experience, and are gratuitously punitive to our patients." Except where we must forbid something for a perfectly definite reason, our patients' likes and dislikes must be carefully considered; whereas it is our own likes and dislikes that tend to appear in our dietetic schemes. Yet it is extraordinary how often quite opposite methods of restriction may do good. A patient goes to a physician, whose opinion is that all purins are deadly poisons. He is put on a purin-free diet and improves. Tiring of the restrictions, he seeks other advice, and finds another physician who holds that most ills are due to incomplete combustion of carbonaceous foods. These are now restricted, while he takes meat freely, and again he improves. The explanation is he ordinarily eats and drinks too much. Variety of diet stimulates his appetite, while the monotony entailed by abstention from so many pleasant things results in his eating less altogether. This must be remembered in estimating the reality of the success claimed for many curious diets. Of recent years there has been a tendency to search for a highly concentrated form of nourishment, with the minimum of waste. This is a fallacy; for the due performance of peristalsis and the avoidance of constipation a certain bulk of material is required, which must be sought in non-absorbable articles, such as cellulose. A certain bulk is also necessary to give a sense of repletion. For the successful treatment of obesity, for example, non-absorbable material is requisite to give satisfaction without excessive assimilation.

It follows from all this that the physiologist looks askance at many of the schemes propounded by the dietetic enthusiast, whom he regards, often with justice, as a faddist of a more or less dangerous sort. The faddist pays no attention to idiosyncrasy, "the factor that changes one man's meat into another man's poison. . . . We do not yet know why one person can eat lobster-salad with impunity while the slightest indulgence in that dainty by another causes a generalised rash that has on occasions been mistaken for scarlet fever."

Special Diets

Certain diets will be considered under the diseases for which they have principally been employed. Thus the purin-free diet is discussed under *Gout*, and the soured milk diet under *Intestinal Intoxications*. Diets for

diabetes, nephritis, oxaluria and phosphaturia, will be found under those headings, and so forth. Certain other diets such as the "whey cure," "grape cure," and "fruit cure," are really disguised forms of partial starvation which have been used for dyspeptic, arthritic and albuminuric gross feeders of sedentary habits. They have not found any great favour in Great Britain, and are mostly resorted to by the Teuton. But reference may be made to certain well-known dietetic systems which have attained some degree of popularity in this country.

The *Salisbury treatment* consists of exclusively protein diet, only fresh, minced lean meat and hot water being allowed thrice daily. The minced meat may be made into the form of a cake lightly grilled. It has been used in chronic dyspepsia with atonic dilatation of the stomach, in chronic gout and rheumatism, obesity, and some skin diseases such as psoriasis. It is recommended that the diet should not be continued for longer than six weeks, when a return should be made very gradually to a moderate mixed diet. It must be remembered that this diet is apt to throw a strain on the excretory organs and is, therefore, definitely contra-indicated if there is any degree of renal inefficiency. I have also known the symptoms of renal calculus to date from the adoption of this diet for obesity.

The *lacto-vegetarian diet* is advised in cases of raised blood pressure, in obesity with constipation, in gastric and intestinal disorders associated with intestinal putrefaction or functional nervous diseases, in insomnia and cardiac neuroses. According to Hutchison, this diet has the following advantages: (1) comparative freedom from purins; (2) the lessening of intestinal putrefaction; (3) richness in mineral salts, and (4) a more bulky residue in the large bowel which tends to correct constipation. It consists of a vegetable diet with the addition of milk and things made with milk, such as junket. It is clear that such a diet can be of considerable nutritive value, and can be made both varied and appetising. It is, therefore, less open to objection than many special diets.

The drawback to a purely *vegetarian diet* is that the human alimentary tract is adapted for an omnivorous diet. The comparatively small stomach and the meagre size of the cæcum are anatomical points against the suitability of strict vegetarianism. The claims made by vegetarians as to the immunity they obtain from diseases such as appendicitis and cancer are unsubstantiated. Moreover, it is clear that certain diseases such as beri-beri, pellagra, sporotrichosis and tapeworm are acquired from vegetables. One of the principal fallacies in vegetarianism is the assumption that the chemical composition of the food is the same thing as the amount of nourishment assimilated from it, whereas the percentage absorbed is far higher in the case of an animal diet, a large proportion of the vegetable protein and the cellulose simply passing through the intestine.

A *fruit diet* is only another variety of vegetarianism. Though pleasant for warm climates and though superior in energy value to a purely vegetable diet, it is open to the objection that it contains such a high proportion of carbohydrate and that the palate soon tires of so much sugar. It is, however, a useful variant for one meal in the day, such as lunch. As Leipoldt says, "a bunch of well-selected Malaga raisins and a small tumbler of milk make an ideal luncheon, which possesses all the requirements necessary for repairing the body waste and are an excellent change from a ham sandwich and a glass of beer, which contain approximately the same amount of nutritive material."

Methods of Under-nutrition.—Certain diets, such as Banting's and Tuffnell's, frankly aim at under-nutrition and partial starvation.

The essential feature of *Banting's diet* is abstention from bread, milk, butter, sugar and potatoes. It is as follows—

Breakfast.—Four to five ounces of beef, mutton, kidneys, broiled fish, bacon or any cold meat except pork; a large cup of plain tea, and a little biscuit or one ounce of toast.

Dinner.—Five to six ounces of any lean meat or fish, any vegetable except potatoes, one ounce of dry toast, some fruit out of a pudding, any kind of poultry or game, and two to three glasses of good claret, sherry or madeira.

Tea.—Two to three ounces of fruit, a rusk or two, and a cup of plain tea.

Supper.—Three to four ounces of meat or fish, as at dinner, and a glass or two of claret.

It will be noted that this diet is largely protein in character and is, therefore, subject to the same limitations as the Salisbury treatment. Banting himself lost 35 lb. in thirty-eight days on this diet.

Œrtel's system is somewhat similar except that the consumption of fat is restricted more than that of carbohydrates, and great stress is laid on limitation of fluid. (For other dietetic schemes in obesity, see article on *Obesity*.)

Tuffnell's diet was formerly largely used in the treatment of aneurysm in combination with absolute rest. It consists of 4 oz. of bread and butter, 2 or 3 oz. of meat, 4 oz. of milk and 3 or 4 oz. of claret daily. Later observers usually omitted the alcohol but restricted the fluids to 10 oz. daily. It is doubtful whether such a restricted diet is either wise or efficacious. The late Hilton Fagge preferred in his own case to work quietly

as long as he could, regarding this treatment as worse than the disease. The recognition of the large part played by syphilis in the production of aneurysm has led to the practical abandonment of Tuffnell's diet, most authorities preferring a simple, moderate restriction of fluid combined with anti-syphilitic remedies. Kingston Fowler has pointed out the special dangers of Tuffnell's diet when aortic regurgitation is also present.

Some popularity attaches at the present time to the adoption of a régime of absolute starvation, nothing more than water being taken. From conversation with those who have tried both, I conclude that after the first forty-eight hours complete starvation causes considerably less discomfort than a meagre and inadequate diet. Certainly a brief course of starvation seems definitely to have benefited patients suffering from asthma, gout, and various gastric and intestinal disorders. Guelpa's method of complete starvation for five or six days and even more, combined with free drinking of purgative waters has acquired a considerable popularity in certain quarters in the treatment of intestinal intoxications, "sluggish liver," high blood-pressure, chronic arthritis, myalgia, diabetes and obesity. My own experience of it is limited, but I have met those who have expressed themselves strongly as to its value, and it really does not cause serious inconvenience. Such drastic means can, however, seldom be required and are rarely advisable.

Methods of Over-Nutrition.—Other methods aim at definite over-nutrition. Some time ago forced feeding was adopted almost as a routine in sanatoria for consumptives. It has now, however, been abandoned, for although it was found a comparatively easy matter to make a phthisical patient accumulate a considerable quantity of fat, this did not necessarily mean that the disease was checked, and it was even thought that the carrying about of such a mass of inert material was a positive disadvantage. Moreover, the weight is certain to decline as soon as forced feeding is stopped, and this has an unfavourable influence on the patient's mind. In the *Weir-Mitchell treatment* there is also an attempt at over-nutrition, though isolation, rest and massage are also essential features. Fresh milk is given at first every two hours from two to four pints daily, and may be increased even to ten pints. Later on farinaceous food, such as arrowroot or cornflour, and then lightly boiled eggs, fish, chicken, game, red meat and bread and butter as the digestive capacity improves, until the patient can take three full meals a day combined with the same amount of milk partly with the meals and partly between them. This method has been employed with success in the treatment of neurasthenia.

TABLE I.—ORIGINAL LENHARTZ DIETARY

Days	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Eggs	2	3	4	5	6	7	8	8	8	8	8	8	8	8
Sugar, with eggs (in grammes)	—	—	20	20	30	30	40	40	50	50	50	50	50	50
Milk (in cubic centimetres)	200	300	400	500	600	700	800	900	1000	1000	1000	1000	1000	1000
Raw scraped beef (in grammes)	—	—	—	—	—	35	70	70	70	70	70	70	70	70
Milk rice (in grammes)	—	—	—	—	—	—	100	100	200	200	300	300	300	300
Rusk (soaked), 1 piece = 20 grammes	—	—	—	—	—	—	—	1	2	2	3	3	4	5
Raw ham (in grammes)	—	—	—	—	—	—	—	—	—	50	50	50	50	50
Butter (in grammes)	—	—	—	—	—	—	—	—	—	20	40	40	40	40
Represents in calories	280	420	637	777	956	1135	1588	1721	2138	2478	2941	2941	3007	3073

TABLE II.—DIET DURING FIRST SIX DAYS OF LENHARTZ TREATMENT

Day.	Eggs (drachms per hour).	Milk (drachms per hour).	Sugar (*per diem*, added to eggs).
1	2	4	—
2	3	6	—
3	4	8	1 oz.
4	5	10	1 oz.
5	6	12	1½ oz.
6	7	14	2 oz.

LENHARTZ DIET IN GASTRIC ULCER

In view of the interest which has recently been taken in the Lenhartz diet in the treatment of gastric ulcer, it is advisable to give the exact method employed. The question is further discussed in the article on *Diseases of the Stomach*. Lenhartz maintained that the principles which should guide us in the treatment of gastric ulcer are (1) administration of sufficient food to maintain the patient's nutrition, but at the same time to prevent distension of the stomach, which would occur if a quantity of milk adequate to maintain nutrition were given; (2) a diet rich in protein, which fixes the hydrochloric acid by combining with it and thus prevents its influence in continuing the ulcerative process. Bolton has shown clearly that hyperacidity is a potent

factor in preventing the healing of gastric ulcer. Lenhartz thought these indications were best fulfilled by giving small quantities of beaten-up egg and milk, both of which are kept iced. In that way a diet rich in albumen is obtained and distension of the stomach avoided. His plan is to feed the patient by teaspoonfuls every hour from 7 a.m. to 10 p.m., allowing rest throughout the night. Table I gives the original Lenhartz dietary, and Table II shows what that dietary means in teaspoonfuls per hour for the first six days. On the first day the patient is to have two eggs and 200 c.c. of milk, and that means he has two teaspoonfuls of beaten-up egg and four teaspoonfuls of milk every hour. Sugar is added to the eggs on the third day. On the sixth day he gives some raw scraped beef. I think the creatin in the beef is an objection, as it tends to stimulate the secretion of acid, and, therefore, in my cases, I have substituted an equivalent amount of cooked minced chicken. By the seventh day he is taking a little rice, and on the eighth day some soaked rusk. On the tenth day he is having raw ham, according to Lenhartz. That probably suits the German patient, but the English patient does not relish it, and I have simply increased the amount of minced chicken. He recommends an ice-bag being applied to the epigastrium, but I have not often used that. He also recommends that the bowels should not be opened at all during the first week, in order to avoid peristalsis and to promote absorption of the outpoured blood by the intestines, and then, if necessary, to use a small glycerine enema or one of plain hot water. I have not allowed my patients to go as long as that without opening the bowels because of the amount of straining which is required when constipation has lasted so long. He claims as advantages for this method of treatment that the recovery is more rapid, and that it does not deplete the patient because the food supply is sufficient throughout. The sour regurgitation subsides, vomiting and bleeding cease more quickly and relapse is less frequent, while pain ceases promptly, and morphia is seldom required. Moreover, it is possible to treat anæmia earlier and there may even be an increase in body weight during the first week.

Rectal Feeding.—It is generally admitted now that nutrient enemata, as ordinarily administered, have no nutritive value. I have compared the metabolism of patients on such enemata with those supplied with simple saline solution per rectum and have found them to be almost identical. It is improbable that more than 1 gm. of nitrogen can be utilised in this way in the day, an amount for which it is not worth while submitting the patient to so much inconvenience. It is clear that as the rectum is the main site for absorption of water, the food must be presented in a fluid form, and that nutrient suppositories are therefore entirely useless. But, further, the rectum secretes no digestive ferments and, therefore, anything presented to it must be completely pre-digested. Dextrose is the form in which carbohydrates are absorbed and, therefore, it is not surprising that this appears to be the one ingredient of a nutrient enema which is of value. It is probable that any benefits which have hitherto been obtained from nutrient enemata as ordinarily administered has simply been due to the water, dextrose and salt contained. Five per cent. of dextrose and 0·9 per cent. NaCl is the most convenient strength. A pint of this can be given three times a day by gravitation. The funnel should only be raised high enough above the patient to allow the fluid to pass in quite slowly and in no case higher than 18 inches. It should take not less than 20 minutes to administer one pint. I have carefully investigated the question of absorption of pre-digested fat by the rectum, but could obtain no evidence of its occurrence. As far as proteins are concerned, it is clear that, as they are completely broken down to simple amino-acids before absorption, this is the only form in which it is any use giving them in an enema. When I had satisfied myself of the uselessness of the ordinary nutrient enema, I tried a mixture of amino-acids in the form of Fairchild's enemose. But this did not yield good results, and the metabolism as judged by the output of nitrogen and diacetic acid in the urine appeared to be the same as in starvation. Rendle Short, however, obtained much better results by use of milk which had been incubated with liquor pancreaticus for twenty-four hours. His figures show a larger absorption of nitrogen than any others I have seen. Since then I have given on several occasions two to three pints of pancreatised milk daily on this plan. The incubation has been very conveniently carried out in Thermos flasks. In one case, where any food by the mouth caused pain, and Lenhartz's diet could not be tolerated at all, this plan was carried out with marked success, and with hardly any inconvenience. I still hold, however, that, in the words of the late Dr. Gee, "a little food in the stomach is worth a great deal in the rectum." Also the success of Lenhartz's diet in cases of recent hæmatemesis is sufficiently marked to make it seldom necessary to resort to rectal feeding.

Subcutaneous Feeding. — In cases where all food is rejected both by the stomach and rectum, efforts have naturally been made to find a satisfactory system of subcutaneous feeding. But it cannot be said that apart from filling up the subcutaneous tissues with normal saline solution that these efforts have met with any

degree of success. As proteins have to be dealt with by the liver on their way up from the intestines, it is impossible to administer them or their disintegration products subcutaneously. Indeed, as they may be toxic before the liver has intervened, it is positively dangerous to make the attempt. Moderate quantities of dextrose or levulose may be absorbed from the subcutaneous tissues, but there is great danger of producing sloughing of the tissues. It is possible to give them intravenously, but it must be remembered that they will be readily excreted by the kidney, so that the practical utility of such a method is limited to the use of levulose in diabetic coma. (See article on *Diabetes*.) It is claimed that 30–60 gm. of sterilised fat can be assimilated from the subcutaneous tissues in a day and in cases of malnutrition the simpler plan of getting fat absorbed by inunction has met with some success in infants. For this purpose, it is usual to employ cod-liver oil with the addition of a little grass oil to cover its objectionable odour.

W. L. B.

THE DIETETIC TREATMENT OF INFANTS

In the treatment of infantile ailments dietetic measures often take precedence of everything else. Many an illness, whether acute or chronic, is dependent on overfeeding, or on food which is unsuitable in quality or quantity or is lacking in some essential ingredient. Gastric and intestinal disorders are very common. Rickets and scurvy depend mainly on diet. And in all lung affections the diet is of special importance, for over-distension of the stomach by food or gas presses the diaphragm upwards and interferes with the action of the heart.

It must be borne in mind that the food supplies of the sick child, though smaller in quantity than those of an active child in good health, are the same in general composition. Any modification required is usually a reduction in the quantity and percentage composition of the food, especially if there is fever or alimentary disturbance. In acute illness the digestive capacity is diminished, and a diet appropriate in health may then set up gastric or intestinal disorder. Sometimes pre-digested foods are necessary. A liberal supply of water must be given in febrile states. It is important to avoid the administration of drugs likely to cause nausea or dyspepsia. Apart from such a cause, anorexia and vomiting are the infant's only means of indicating that he does not want food; while diarrhœa and undigested stools show that he is being overfed. Attend to the child's tastes, if they are reasonable. Maternal nursing must be continued during infantile disorders, unless serious illness is due to the mother's milk. If this is lacking in quantity or quality, measures can be adopted to improve the supply, or a wet-nurse may be utilised. The breast-fed infant gets more albumin than one brought up "on the bottle"; and, in the case of the latter, the albumin in the milk is often rendered insoluble by boiling. Moreover, the cooking of milk deprives it of valuable biological qualities; and during illness it is inadvisable to change a food supply which apparently agrees with the child. The quantity of maternal milk can be increased by the ingestion of an extra amount of fluid, preferably nutritious fluid, and by extra food, maltine and somatose; by drugs, such as iron, arsenic and strychnine; possibly by lactagol, an extract of cotton seed; and by stimulation of the breasts by massage or faradisation. The fat-content is increased by a liberal protein diet and malt extracts; the protein-content being increased at the same time. Increased frequency of nursing also increases the total secretion of milk and the protein percentage. Exercise reduces the protein percentage.

Hence, in the case of a breast-fed infant suffering from digestive disturbance, the maternal milk supply must be regulated. Usually, it is advisable to feed the child less frequently. If, on the other hand, the child is suffering from some other illness, it may be advisable to let the breast be given more frequently, say every two hours, because of the small quantity taken at any one time. But do not allow the child to be weaned merely because it is ill.

Should it be necessary to stop breast-feeding, it is essential to put the child on a simple food which he can digest. If he has never had any food except mother's milk, it is unlikely that he will be able to digest the ordinary diluted cow's milk suitable for a child of his age and weight. No absolute rule can be laid down as to what can be digested. It depends so much on the nature of the illness, the size and weight of the child, and his environment. As a general principle begin with a food much weaker in quality than that normally suitable for a healthy infant of the same age and weight. The quantity for each meal need not be altered. Similar principles can be applied in the case of a bottle-fed child who is ill, though the diet need not be altered if it is digested and appropriate, except perhaps that the quality may need reduction. Let us consider, therefore, the common and simpler foods, suitable during illness, and take the least nutritious ones first.

Whey is only slightly nutritive but is easily digested. It contains about the same amount of sugar and salts as the milk from which it is prepared, is devoid of casein and practically free from fat, and contains about 0·85 per cent. albumin. If the curd is squeezed through

muslin some of the fat globules and casein particles pass into the whey, making it richer and more nutritious, but the casein is finely divided and does not form curds in the stomach. Whey is easily enriched by adding cream. The addition of one drachm of cream, 16 per cent. fat, to two ounces of whey is equivalent to adding 1 per cent. fat, besides slightly increasing the protein content of the mixture. Whey is usually made by coagulating milk with rennet, the curd contracting and squeezing out the whey. A simpler method is to buy *Sweet Whey Powder* and add one teaspoonful to two ounces of water: it makes an efficient substitute. Tartrated whey, citric acid whey and white wine whey are sometimes used. The last of these is valuable when stimulants are needed. It is, in my opinion, better to rely on brandy, for the dose can be more accurately regulated. Whey is not always suitable and may give rise to "whey poisoning," a kind of intestinal toxæmia possibly due to a qualitative and quantitative difference in the salts, or perhaps some gastro-enteritis.

Ass's milk is a valuable temporary food, somewhat costly. It is quite as digestible as human milk. Babies do well on it for a short time, but I have never found it of great value for more than a month or two. It is rarely necessary to have recourse to this milk, as some of the proprietary foods are quite as satisfactory for temporary purposes.

Proprietary Foods.—The simplest of these for use during illness are various kinds of condensed milk, Allenbury No. 1 Food and Horlick's Malted Milk. Condensed milk must be given in weak solution to start with, *e. g.* one teaspoonful to two or three ounces of water. The high percentage of sugar in the sweetened brands, such as "Nestlé's" and "Milkmaid," may cause flatulent distension. If so, and in cases of intestinal inflammation or catarrh, give an unsweetened brand, such as the "Ideal," adding sufficient sugar to make it palatable. Or the Allenbury Food may be tried. Sometimes a malted food is more suitable and Horlick's Malted Milk, a condensed milk with maltose added, proves valuable.

Peptonised milk may be better than any of these foods. Use either Fairchild's or Allenbury peptonising powders and make it freshly twice a day. Peptonise the milk for fifteen minutes and give it diluted with an equal quantity of water. If this agrees the proportion of peptonised milk can be increased. Sugar is added in the proportion, one drachm to two ounces of milk and water. Use milk sugar if there is enteric disturbance. Sometimes maltose is preferable, or a teaspoonful of malted milk can be added to each feed. In order to pass from peptonised milk to a diet of milk, sugar and water, either reduce the duration of peptonisation gradually or give one feed a day of the modified ordinary milk, and if it agrees slowly replace the feeds of peptonised milk by the new mixture. Provided the peptonised milk is brought to boiling-point, to destroy the ferment, it will keep for hours and not turn bitter. If more fat is wanted in the diet either use for peptonisation the top half of milk, which has stood for three hours in the cold or add cream to each feed.

Desiccated milks are useful in hot weather and in diarrhœal affections. Some are preparations of pure casein, *e. g.* Biogene, Casumen, Plasmon, Protene and Tilia. Sanatogen is a mixture of casein and 5 per cent. glycerophosphate of soda. The addition of these foods to ordinary milk or whey mixtures is a simple method of increasing the protein percentage. *Albulactin*, a milk albuminate soluble in water, can be similarly added to milk to increase the percentage of albumin. It helps to prevent the formation of large curds. *Sweet Whey Powder* is somewhat similar, but contains sugar in addition. Desiccated whole milk is sold under the names of Glaxo and Lacvitum: and desiccated skimmed milk, as lacumen. Such foods are of temporary value, but they are deficient in fat and antiscorbutic properties, and are far removed from fresh foods.

Cow's milk is the main food of an infant who is not breast-fed. In the case of illness, and even in health, it must be modified to suit the child. Unless the milk is of known purity, especially in hot weather, it must be brought to a boil before it is given to the child. Pasteurisation and sterilisation are rarely needed, and they reduce the antiscorbutic properties of the milk. Uncooked fresh milk is more valuable than any food prepared from milk, but there are certain risks attached to its use. Some infants do well on *citrated* milk, undiluted milk with one grain of citrate of soda per ounce. Although as a rule undiluted milk is unsuitable in illness, citrated milk is sometimes remarkably beneficial, even in intestinal disorders.

The simplest modification is dilution with water or some weak cereal decoction. Egg albumin, gelatine and dextrinised foods are also used as mechanical attenuants. The cheapest mixture is that of milk, water and cane sugar. Barley water can be used as a diluent after the first month of life, provided a very weak solution is used at first and the strength is only slowly increased. Much of the theoretical objection raised to giving barley water, or starch in any form, at an early age has been controverted by clinical experience and recent physiological investigation. Various carbohydrates can be used, such as milk sugar, cane

sugar, maltose, dextrins, lævulose, dextrose and starch, provided the quantity is not excessive.

Apart from simple peptonisation the milk can be partially predigested by the addition of *Benger's Food*. In this process of preparation the proteins in the milk and the starch in the food are partly digested. Such a food, in small amount, may also be used from the earliest months of life. It is most valuable if the digestion is weak and during illness.

Or the milk may be malted. Mixtures of milk, water, cream and Kepler's malt extract are often most digestible. The milk is boiled and cooled to 98° F. before the malt extract is added. So, too, the addition of a malted food, such as Mellin's or Horlick's, renders the mixture more digestible and more nutritious. These foods must only be used in moderation or the child becomes unduly fat: and they must not be given to replace the necessary proteins and fat of milk.

Lactic Acid Milk is not often needed. The protein is in the form of casein lactate. Buttermilk is given sweetened and sterilised. Lactobacilline milk is prepared by inoculating milk with huge numbers of lactic acid bacilli. These bacilli, and the free acid, help to prevent intestinal dyspepsia and limit intestinal putrefaction. They are occasionally of value in enteritis and colitis. For infants, mix the milk with two parts of barley water and add cane sugar, half an ounce per pint; for older children give equal parts, or two of milk to one of barley water. Obviously the general diet of the infant during illness is one of milk in its most digestible forms, and carbohydrates. Fats must be given in moderation. Cream is often unsuitable, especially if centrifugalised or containing preservatives. If extra fat is needed, it can be given in the form of olive oil, cod-liver oil, butter, margarine or dripping. The addition of a little yolk of egg is of great value in wasting disorders, for the sake of its fat, iron, lecithin and other constituents. In scorbutic conditions, and all infants fed for a prolonged period on a cooked diet, give fruit-juice in the form of sweetened grape-juice or diluted orange-juice. If necessary, a little potato cream can be added to the milk and vegetable soups may be given.

Meat preparations are rarely necessary. Most of them consist chiefly of salt, water and extractives. Meat jellies, though expensive and innutritious, stimulate the appetite and aid digestion. Small quantities of beef-tea, chicken-tea, etc., are similarly useful. They relieve the maternal fears of starvation, and are valuable especially for fat, plethoric babies in whom it is advisable to reduce the calorific value of the diet.

During the *second year of life* dietetic treatment is carried out on similar lines, but more variety is permissible in the way of carbohydrate foods, puddings, vegetable purées, mashed potatoes and gravy, eggs and fish, and even meat if the child is old enough. At this period, just as in younger infants, the essential principle is to give a sufficiently nutritious diet, palatable and digestible, without overfeeding the child. Well-nourished infants can live on a very limited diet during illness, especially febrile disorders, for many days at a time and with great advantage.

General Directions

For Infants.—Feed every two hours during the first month, from 5 a.m. to 11 p.m.; every two and a half hours during the second month, from 7.30 a.m. to 10.30 p.m., giving also one feed during the night, preferably between 4 a.m. and 5 a.m.; every three hours after the second month from 8 a.m. to 11 p.m. and one feed during the night. After the sixth month, sometimes earlier, and perhaps in cases of indigestion, the child may be limited to six feeds at three and a half hourly intervals, or to five feeds at four hourly intervals.

In artificially-fed infants the frequency of feeding should be the same, and the composition of the food as follows—

In the *second month:* milk 1 oz., water $1\frac{1}{2}$–2 oz., lactose 1 dr. In the *third month:* milk and water, equal parts, 3 oz., lactose 1 dr. Each feed may then be increased slowly by $\frac{1}{2}$–1 oz. a month, up to a total of 5–6 oz. at six months of age. After this the meals may be made stronger by giving more milk and less water in each feed. Cream must only be added in moderation during illness. Barley water may be given instead of water after the third month, or even earlier if it is very weak. In the ninth month, sometimes earlier, the child may be trained gradually to digest more carbohydrate food by giving a malted food, such as Mellin's or Horlick's, next a partly malted food such as Savory & Moore's, and then rusks or Robb's biscuits ("tops and bottoms") crumbled up in milk. During illness it is rarely advisable to give other foods in the first year of life, except in so far as the addition of fruit juice or yolk of egg may be advisable. Even in the second half of the first year a similar diet is generally appropriate in illness, but it can be varied by giving Benger's food, potato and gravy, custard or other milk pudding, bread and milk, biscuits, and bread and butter.

Diet at 12–18 *months of Age.*—6–7 a.m.—Whole or diluted milk, hot or cold, 6 oz., with rusk, stale bread or bread and butter.

8.30–9.30 a.m.—*One of these daily:* a small basin of rusk or bread and milk: of fine oatmeal porridge, Quaker oats, Grape nuts, etc., with

cream or milk; thick milk gruel; or thin milk cocoa with bread and butter or bacon fat.

12.30–1.20 p.m.—*First Course :* a teaspoonful to a tablespoonful of mashed potato or stale bread crumbs, with red gravy, meat juice, chicken or mutton broth, or the yolk of a lightly boiled or poached egg.

Second Course : A tablespoonful of custard, tapioca, ground rice, fine sago, cornflour or semolina pudding, junket, cornflour mould or blancmange. A little fruit juice occasionally. Cold water or milk and water to drink.

4.30–5.0 p.m.—Same as first meal; or thin cocoa with bread and butter, treacle or honey, rusks and plain biscuits.

8.0–9.0 p.m.—Milk gruel 6 oz., Benger's or Mellin's Food; rusk, sponge finger or bread soaked in milk.

Diet from 18–30 *months of Age.*—The child should be fed at the same times and on about the same quantities, the amount depending on the appetite and state of health. For breakfast a lightly boiled or poached egg with bread and butter may be given, alone or as a second course, or bread soaked in bacon fat. For dinner, boiled fish, up to one tablespoonful can be given, pounded up at first, at fifteen to twenty-one months of age. After the child has taken fish for two or three weeks he may have pounded-up chicken and then red meat. These foods must be given with mashed-up potato and greens, at first passed through a sieve. Thus, a suitable diet includes for dinner: egg twice, white meat twice, red meat twice, and a thick vegetable soup once a week. Or, when the child is taking an egg occasionally for breakfast, the first course at dinner should consist of fish, white meat and red meat, each twice a week, and on the odd day a thick vegetable soup, brains, calf's head or sweetbread. Water or barley water may be drunk. At this age baked apple can be given, and stewed fruits free from skins, pips and stones, or mashed-up ripe bananas. E. C.

THE NON-OPERATIVE TREATMENT OF MALIGNANT DISEASE[1]

The treatment of cancer may be considered under two headings—

I. Preventive and curative efforts.

II. Palliative efforts.

These are not distinct from each other. Some efforts at cure relieve symptoms and prolong life. On the other hand, some curative efforts produce pain and discomfort. The use of particular remedies that have this effect should always be considered in terms of the chance of cure in the particular patient concerned.

For the reason that it is the duty of the practitioner to consider first whether or no a disease can be cured, and then, if it cannot, to what degree it can be palliated, the treatment of cancer will be here dealt with in this order. Such a plan necessarily involves the mention of forms of radical treatment that are at present under trial, and of others that have little more than historical or theoretical interest. In a practical treatise such as this much space cannot be devoted to either of these modes of treatment. At the end of this article will be found a scheme of practice in which the treatment will be summarised for different types of case, and due regard will there be given to those measures known by experience to be really helpful rather than illusory.

I. Preventive and Curative Efforts

Curative efforts are either (1) Rational or (2) Empirical.

1. Rational Efforts are based upon some central idea. There are four of these central ideas.

(1) *The idea that cancer is due to errors in tissue metabolism capable of correction by a diet specially chosen.*—It has been thought likely that an association exists between uric acid retention and cancer. And as a "purin-free" diet is by some considered to prevent uric acid retention, these authorities have urged the adoption of such a diet in the treatment of cancer. Trial of such a diet has recently been made in a number of selected cases at the Cancer Hospital, with equivocal results. It was difficult to persuade the patients to submit to the diet, especially in face of loss of weight and general tone resulting from the experiment. It is difficult also to feel convinced of the soundness of the argument underlying the treatment, for the close association of gout and cancer is by no means proved. Even if it were true that cancer developed more readily in patients who ingested purins this would seem to be merely a predisposing cause, to remove which would still leave us far from curing the disease.

By some observers cancer has been thought to be due to the "demineralisation" of foods, as by the use of white flour and of peeled potatoes. Such food defects, if real, could easily be remedied by a full allowance of fresh fruit, by using wholemeal bread and by cooking potatoes in their skins. The "demineralisation" theory runs parallel with the notion that cancer is due to the relatively low content of potassium salts

[1] A brief reference will be made in this article to those surgical measures other than radical procedures which may be undertaken for the relief of patients suffering from cancer. A more inclusive title would be "the treatment of non-removable malignant disease," but if "non-operative" be taken to mean "non-removable" the more common title may still be used.

in the body; it is claimed by some that free administration of potassium salts has cured cancer. Two considerations arise—the first, that it is easy to add potassium salts to whatever treatment of a more convincing sort a cancer patient is having; the second, that the condition most often resembling cancer is gumma, and it may be that the cure of gumma by administration of potassium iodide has led to this notion that potassium salts cure cancer.

An idea of a different and more convincing kind, which may be dealt with under this heading, is that put forth by Dr. Monckton Copeman, and worthy of thorough trial. Dr. Copeman suggests that the cancer cell might undergo retrogressive changes if the tissues were denied those active principles in food termed *vitamines* by Funk. These vitamines appear to constitute the nutritive factor in food, without which such "deficiency diseases" as scurvy are produced. Young and embryonic tissues are specially dependent on these substances for their growth. Removal of them from food, by the use of the autoclave, might conceivably lead to recession of the new cancer cells, the healthy tissue remaining relatively unaffected. This hypothesis is now being tested on as large a scale as is practicable.

(2) *The idea that specific immunity to cancer can be established in a manner analogous to infective processes.*—It is hoped that either by the use of an anti-serum or of a vaccine the patient may acquire passive or active immunity to the disease. The procedures follo very closely upon those adopted for known microbic infections. Despite a large number of trials, little or no success has attended either of these methods in human cancer.

(3) *That the cancer cell is more readily destroyed by certain toxic agents than are the cells of the host.*—This is the principle underlying the great majority of the efforts made to cure cancer. We cling to the fact that the cancer cell, in its hasty nutrition and disordered growth, is a less stable thing than the cell which it is replacing. It should therefore be capable of more easy destruction. The natural history of the cancer cell supports this principle, and the inherent tendency of these cells to autolysis within the tumour suggests the advisability of trying by all legitimate means—legitimate, that is, with reference to the tissues of the host—to precipitate this destruction. The various toxic agents that have been used to compass this desire fall into two groups: *microbic toxins and ferments*, and *drugs*, chiefly certain preparations of the heavy metals. If we regard the chief and the ultimate action of radium and of X-rays as of a chemical nature we must include these measures also under this principle, but this view of the action of radiations is by no means proved; moreover, in the present state of our knowledge it is more convenient to consider radiation treatment separately.

(*a*) **Microbic Toxins and Ferments.**—Into this class of remedies come Coley's fluid, *Micrococcus neoformans* and "anti-meristem." The disappearance of sarcomata under the influence of an attack of erysipelas was the pioneer observation which led to treatment by *Coley's fluid*. The writer's experience of Coley's fluid, both of the market virus and of material specially made, has been disappointing. Considering the fact that this material has now been in use for more than twenty years, the infrequency with which the treatment is embarked upon to-day suggests that other observers are equally discouraged by their results. The desirable effects upon the tumour seem to be in direct proportion to the degree of general toxicity produced, and without this general result the local effect does not follow. The pain and discomfort endured by the patient create, in England at all events, an almost overwhelming objection to the treatment. So much so that few patients have the courage, and few practitioners the conviction, necessary to pursue the method very far. The writer recently endeavoured to raise the resistance of patients to the general effects of the fluid by preliminary inoculation with S. pyogenes vaccine, but the results were not encouraging. It is possible that in conjunction with other methods, such as radiations and arsenic intravenously, doses of the fluid of lesser size than those producing such acute suffering may be helpful. It seems clear that it is only in cases of sarcoma that results are to be expected from the use of Coley's fluid.[1]

Micrococcus neoformans has been used as a vaccine and also to prepare a serum (Doyen's serum). Neither application has proved of service in the cure of cancer. As it now seems proved that this micro-organism is really Welch's *Staphylococcus epidermidis albus*, it becomes obvious that its use as a vaccine might well alleviate certain symptoms due to secondary infection of a tumour, or (especially) of a malignant ulcer. And this alleviation, which undoubtedly occurs in some cases, may have led to the assumption that these preparations cured cancer just as the finding of the micro-organism in the growth led to the assumption that it was the cause of cancer. This form of treatment must therefore be relegated to the list of palliative measures merely.

Antimeristem (Schmidt) appears to be a derivative of a mucor, and has been much advertised of late. The evidence of its beneficial action appears to rest as yet almost solely upon the observations of its inventor.

[1] For directions see Summary.

Diastasic ferments have been largely used, and trypsin has had the longest vogue amongst this class of remedies, on the basis of some observations by Shaw-Mackenzie tending to show that the antitryptic power of the serum is high in cancer patients. Shaw-Mackenzie advocated the subcutaneous injection of trypsin together with the administration of pancreatic extract, duodenal extract and bile preparations by the mouth. This treatment seems of late years to have been largely abandoned.

Allied to the enzymes, perhaps, are certain substances formed in exudates and transudates occurring intercurrently in cancer patients. It has been noticed that on rare occasions cancer resorbs coincidently with the resorption of such exudates. This observation led to the treatment of cancer by injection of the exudate in increasing quantity, both in the patient from whom it has been removed and in other patients. With the same idea to guide them some observers have used blood serum, or blister fluid, for a similar purpose. The writer's experience of such methods is quite negative, and no authentic cases of actual recovery seem available for reference.

(*b*) **Drugs.**—The second group of toxic agents used to destroy cancer cells include chiefly the heavy metals and their compounds. The brilliant work of Erhlich and his colleagues in connection with the spirochæte of syphilis has breathed fresh life into the flagging body of chemicotherapy, and has incidentally given a new stimulus to research in cancer treatment. A large amount of material provided by many thousands of mice successfully grafted with cancer has been available for this purpose. The highly selective action of various substances upon particular cells has led to the trial of many products specially synthesised by the chemist for the purpose.

Wassermann and others have worked specially with the metals of the sulphur group, and have definitely proved that it is possible to cause the complete resorption of mouse cancer of a certain size by repeated intravenous injection of such a compound as selenium-eosin. Eosin was chosen as part of the metal compound on account of its intensely penetrating character. The demonstration that the cancer cell can be picked out for saturation and ultimate destruction, to the exclusion of the cells of its host, by such means as these, constitutes one of the most significant and encouraging discoveries of recent months. Whether such compounds have any similar effect in human cancer remains to be seen. The choice of the actual compound used is, from analogy with the arsenical preparations employed in the treatment of syphilis, of great importance, and the most efficient preparation—one giving highly toxic effects upon the cancer cell, and relatively low toxic action upon the healthy tissues—may require much exhaustive experiment for its elaboration. Other observers have recorded good results in mouse cancer from the use of tellurium and from selenium given by the mouth. *Copper in colloid form* is also on trial and in this country Herschell and others have recorded what they regard as promising results (see Summary). The silicates have had very extensive trial, in the form of simple sodium and potassium salts given by the mouth, at the hands of Zeller and others; and even Czerny is undecided as to whether there is not some curative effect observable from long-continued use of these preparations.

(4) *The idea that radio-activity can produce retrogressive changes in the cancer cell.*—Of all the methods of dealing with inoperable cancer the two that have most success to place to their credit are undoubtedly X-rays and radium. For the treatment of cancer which is inaccessible to the surgeon, for local recurrences and metastatic deposits and as preventive measures against recurrence generally, they are the most helpful modes of treatment available. It is probable that the nature of the action of both remedies is the same, but it is as yet unknown of what this action really consists. The simple view that the radiations merely destroy the cancer cell because of its lower resistance to all destructive processes is hardly likely to be correct, for it can be shown that X-rays perseveringly applied to the body generally, omitting the tumour, lead to a marked diminution in its size. Nor is it likely that the equally simple view that the radiations merely stimulate the healthy tissues to throw off the parasitic cell is any nearer the truth. The action is probably much more complex than either of these explanations suggests. It has recently been suggested that radiations act by inducing chemical analysis within the cancer tissue, as by liberating choline from lecithin, the choline acting in toxic fashion upon the cancer cell. This notion has led to the direct employment of choline by injection. Of late the production of "secondary radiations" within the body has been under consideration, as it is reasonably hoped that the selective action of the method may be thereby enhanced. Knox draws attention to the possibility of utilising the iron of the hæmoglobin in this way and finds better results from radiation treatment when the hæmoglobin is high than when it is low. It may be possible, by combining radiation treatment with such a method as the intravenous injection of metallic copper or selenium to obtain a similarly enhanced effect by the production of "secondary radiations." The consideration which perhaps appeals most disappointingly in respect of the radiation treatment of cancer,

and which makes it doubtful if we can expect from it much more than we have already got, is the great range of the therapeutic use of the remedy. The very fact that radiations are of great service in other diseases seems to impose a limit upon any very selective efficacy in dealing with the cancer cell. That radiations can cause a tuberculous gland to resume its natural size, and a lymphadenomatous one also, and can so effectually reduce the size of a leukæmic spleen, seems to argue against that power of specialised effect which we feel essential in a means of cure of so specific a disease as cancer. In this place, however, these considerations can but be mentioned. It is hopeful to note that there are, in the minds of the experts, advances still possible in technique and in choice of methods, so that we have probably not yet touched the limits of the practical application of either X-rays or of radium.

For the actual technique of the employment of these remedies reference must be made to the special article dealing with them. It may here be said that in the choice of the actual method—whether X-rays or radium—several considerations apply, especially the situation and size of the growth, and whether or no it is ulcerated. Briefly, it may be said that radium is of special value in tumours of the mouth, pharynx, œsophagus, rectum, vagina, uterus and bladder. Also for small and ulcerated growths and where it is possible to introduce the radium into the interior of the tumour. Coincidently, it must be remembered that X-rays are easier of application in general and much less expensive. Should radium emanations prove useful when taken into the body as radium-water the difficulty of widespread application will be overcome, as also, probably, will the difficulty of expense.

Certain *principles of treatment* laid down by Finzi, both for X-rays and for radium, may be quoted in this place; they are as follows—

(i) Use maximal doses.
(ii) Repeat as frequently as is safe.
(iii) Use sufficient filtration.
(iv) Treat thoroughly, not only the growth itself, but any region it is likely a metastasis might exist.
(v) Continue the treatment after all traces of disease seem to have disappeared.

2. Empirical Measures.—Of these little need here be said; their very name is legion. One or two call for remark because of their occasional advocacy by reputable authorities. *Alnus Glutinosa* (common alder) was introduced by Dr. Underwood Gray, who claimed to obtain good results by the use of a liquid extract from the leaves, administered by the mouth. Under observation at two institutions for the treatment of cancer, negative results were obtained, but with this, as with all other empirical measures, it must be remembered that the cases submitted for trial are necessarily well advanced. *Violet leaves* appear to have less claim to consideration. Treatment by *internal secretions* of various organs seems rational, as in Fouler-ton's suggestion that thymus extract should be tried because the thymus may contribute to the immunity of young animals to cancer. Extracts from the *thyroid gland* and from the placenta have also been freely used.

In respect of all reputed remedies in the cure of cancer it must always be remembered that to disregard the fundamental criterion is but to confuse the issue and to delay progress—reference is here made, of course, to the proof of the diagnosis. Absence of histological evidence, however brilliant the result of treatment may appear, always calls for the exercise of forbearance and generally for a decision to remain silent.

II. Palliative Measures

The practitioner in charge of a case of inoperable cancer is only helped directly by what is practical. Some theoretical considerations have been unavoidable in the preceding section, because in the present stage of our knowledge it is imperative to weigh the pros and cons of so-called curative measures, and some of these are highly theoretical. When faced with daily treatment, however, it is the essentially practical measures that count, and the bulk of these are unfortunately palliative only. But there are really very few cases in which there is nothing to do except to negotiate euthanasia, though in the great majority of cases this stage of the treatment arrives sooner or later.

As already stated, if either of the efforts at cure be attempted it is desirable to choose those means which carry with them relief of distressing symptoms. I am fully convinced that *the most satisfactory line to adopt in nearly all cases is a combination of several different measures;* not in a state of panic, but with deliberate choice of a programme. Thus, faced with an inoperable sarcoma, it might be good to lead off with an alternating treatment by X-rays and radium, and, as an additional measure, to give two or three doses of salvarsan intravenously at weekly intervals during a period immediately following the radiation treatment. In dealing with one of the most common of all types of case—that of a woman who has had a cancerous breast removed and who has developed local recurrence that is inoperable, X-rays and radium may again be employed; vaccines should be employed if there is any secondary infection, the diet should be regulated on the lines indicated, and general tonics, with full doses of iron, should be employed.

The question is often raised whether any preventive treatment should be employed as a *post-operative* measure, as by radio-activity. Some authorities recommend that the scar region be treated by radiations for some weeks following the operation, and this is probably advisable. To keep the wound deliberately open for a time and to subject it to X-ray or radium applications, though a practice obtaining in certain continental cliniques, has not found favour in this country.

Palliative Surgical Procedures deserve some mention here. They are frequently of considerable service and are probably less frequently undertaken than should be the case. Rowntree has recently drawn attention to the alleviation of suffering and the prolongation of life that would undoubtedly follow such procedures in selected cases. It should be remembered that secondary changes in tumours play a considerable part in the distress of the patient, especially in the case of growths in the mouth, breast and uterus. Sloughing, disintegration of the tumour mass, discharges, septic absorption and hæmorrhage—these are the complications that can sometimes be modified or actually cured by timely and discreet surgical measures. The best method of partial removal of such fungating masses, and of otherwise clearing sloughing areas, is probably by the knife wherever possible. A method of recent introduction, and which seems very successful in certain cases, is by *diathermy*. The method appears of special service in growths situate in the mouth, rectum and vagina. The apparatus employed produces a high-frequency current of great power. One of the two electrodes is wrapped in wet towels and is placed on the patient's chest, the other is provided with a metal end and is plunged into the growth. The intense heat thus produced in the tumour mass rapidly destroys the tissue. Harmer briefly gives the details of treatment as follows: "The growth must be sponged so that it is quite dry; the electrode is plunged into the growth and the current is turned on for three to five seconds. A series of punctures is made so that every part of the growth is attacked. There should be no bleeding even with vascular tumours."

This method by diathermy will probably replace the use of the actual cautery for such purposes whenever the requisite current is available. Where it is not, resource may be had to the older method, assuming the knife is not adequate. In no case is it advisable to trust to chemicals (caustics) for the partial destruction of these fungating or sloughing growths. Indeed, the use of strong chemicals is at all times undesirable in treating cancer.

Into the same category comes a class of case in which the indications for non-radical surgical treatment are clearer and more often undertaken. Reference is made to such procedures as gastrostomy for œsophageal cancer, gastro-enterostomy for irremovable growths of the stomach, colotomy for inoperable malignant obstruction to the large bowel and cystotomy for similar obstruction to the bladder or urethra. With these procedures may be put the operation of lymphangioplasty for limbs embarrassed by lymphatic obstruction.

The Treatment of the General Health.—This is of great importance, inasmuch as upon the maintenance of the general tone in large measure hangs the progress (whether slow or rapid) of the disease. Plenty of fresh air is advisable, and if an actual *open-air* life is possible without adding to the mental distress induced by the knowledge of the nature of the disease (should this be known) so much the better. In the cases in which secondary microbic infections are present, open-air treatment is specially indicated. *The diet, pace* those authorities who consider meat-eating answerable for the disease, should be liberal and varied, and should contain articles rich in potassium salts (raw fruit, potatoes cooked in skins, wholemeal bread and uncooked milk). *Tonics* are indicated, and if the patient is receiving radiations as part of the treatment, certain metallic preparations should be given with the idea of inducing secondary radiations in the body (iron, manganese, arsenic). Potassium salts may well be added.

The Relief of Pain.—A careful consideration must be given to the probable cause or causes of the pain so as to select the most appropriate measures for its relief. The fact must not be lost sight of that *radiations* act ofttimes by relieving pain, even in their application to parts not immediately invaded by the growth.

Failing any or much benefit by this treatment, the possibility of relief by *division of affected nerves* must be considered. Division of the lingual nerve sometimes gives great relief to the pain of cancer of the tongue, and the division of the sensory roots of the spinal nerves supplying affected areas in the limbs and trunk is occasionally rewarded by a good result. This indication presents itself chiefly in those cases in which there are unbearable paroxysms of sciatic pain in connection with pelvic growths pressing on the lumbo-sacral plexus.

Attempts have been made to produce degeneration in sensory nerve trunks by the *injection* of various fluids, especially *alcohol* (80 per cent.). The method is only of limited application. More recently, intraspinal injections of analgesics have been attempted for the relief of pain in the type of case just mentioned, and it is well worthy of trial.

The local Application of Anodynes to painful

parts is not of much service, unless these are ulcerated, in which case very weak solutions of eucaine and adrenalin (1 in 100 and 1 in 1000 respectively) in a mild antiseptic ointment is perhaps the best application.

Some form of **drug medication by mouth** becomes imperative, sooner or later, in many cases of inoperable cancer. Certain of the coal-tar products should be tried first, such as *aspirin* (gr. x–xx), or *phenacetin* (gr. v–x), or *antipyrin* (gr. x–xv). Pyramidon (gr. v–x) is a valuable adjunct of more recent introduction. An "antineuralgic" mixture may be tried, such as—

℞ Tinc. Gelsemii ♏ x–xxx
Caffein Citratis gr. v
Acid Nitrohydrochlor dil. ♏ v
Syr. Aurantii ʒ ss
Ex. aq., sextis horis.

But in the majority of patients the use of some preparation of opium becomes inevitable. *Nepenthe* and *liq. opii sedativus* (āā ♏ x–xxx), are perhaps the most useful for oral administration, a route which should always be chosen before resorting to hypodermic medication. Ultimately this latter usually becomes necessary if pain is a marked feature of the case, and in slowly increasing doses.

The *mental state* is perhaps one of the most difficult of the problems of inoperable cancer to face the practitioner. The attitude of the patients varies so much that it is not easy to offer advice. The personality of the doctor and the philosophy of the patient are the medicines of greatest avail. Two lessons experience soon teaches: that not every patient who "wants to know the truth" is prepared to hear it, sometimes he least who asks most boldly; and that self-deception is not seldom a valuable analgesic well worth preserving.

The Treatment of Ulceration, Discharges and Hæmorrhage.—Reference has already been made to the function of partial surgical procedures and of methods of cauterisation in this connection; also to the use of vaccines. It frequently happens that direct applications are necessary to check or to control *offensive and irritating discharges.* The two most useful preparations are *Sanitas* (1 in 20 to 40) and *peroxide of hydrogen* (10 vols.). Dry dressings are preferable to moist, unless there is considerable tenderness and local pain, when warm fomentations are comforting.

In uterine and vaginal cancer, the introduction of *acetone* every four or five days after an initial curetting has in some hands given good results. Care must, however, be taken to prevent the action of the drug on healthy parts, as this produces pain. For this reason the lithotomy position should be adopted and a large-sized speculum introduced.

In the *mucous discharge* complicating œsophageal cancer, the administration of belladonna in small doses may produce considerable relief.

Hæmorrhage, if of the frank variety and from an ulcerated vessel of some size, must be met by ligature of the vessel in its healthy course. This proceeding sometimes leads to retrogressive changes in the tumour, and may therefore be undertaken as a preventive measure. If the bleeding is of the nature of general oozing, the use of the actual cautery or the curette to the ulcerated surface is indicated.

Summary of Treatment in Inoperable Cancer

I. General Principles.

1. Combined methods of treatment lead to better results than single methods.
2. Combinations should be effected both in regard to the destruction of the cancer cell and in regard to improving the vitality of the tissues.
3. If improvement follow treatment consider if the disease be not now amenable to radical cure by operation.
4. Continue treatment after apparent resorption of the growth in all cases.

II. Scheme of Treatment.

1. *Efforts at cure.* Consider applicability to particular case of—
   (1) Radiations.
   Radium in small growths, ulcers, superficial tumours and cancer of mouth, pharynx, œsophagus, rectum, uterus and bladder.
   X-rays in large growths, deep-seated masses and diffused invasions.
   (2) Coley's fluid in sarcoma.
   (3) Intravenous injection of colloid copper or selenium.

2. *Efforts at palliation.* Consider, in each case, the indications for—
   (1) Partial surgical procedures.
   (*a*) For removal of the tumour—by the knife, by diathermy or by the actual cautery.
   (*b*) For the relief of symptoms—by gastrostomy, gastro-enterostomy, intestinal anastomosis, colotomy, cystotomy, tracheotomy, lymphangioplasty.
   (*c*) For the control of hæmorrhage and discharge—by curetting or by the cautery.
   (2) Supporting the general health—by fresh air, good food, abundance of potassium salts, tonics (especially iron), and, in secondary infections, by vaccines.

(3) Relieving pain—by reducing secondary infections, by local anodynes, by division of affected nerve trunks or by injection of alcohol, by intraspinal anæsthesia and by drugs (aspirin, phenacetin, antipyrin, caffeine, gelsemium, pyramidon, but usually by some form of opium—nepenthe, liq. opii sedativi or injectio morphinæ).
(4) Checking secretion of mucus by use of belladonna.
(5) Controlling discharges—by vaccines and by local antiseptics (especially Sanitas and hydrogen peroxide).
(6) Treatment of mental state.

T. J. H.

X-RAY THERAPY

Generally speaking, X-ray Therapy, since the introduction of accurate technique, has been giving much more satisfactory and more consistent results.

In the scope of this article it is not possible to discuss in detail all the varied conditions in which the X-rays have been employed as a therapeutic agent.

There are very few diseases in the treatment of which the X-rays have not been tried with varying success. The literature of X-ray Therapy has assumed considerable proportions, and while there are still differences of opinion as to the best method to employ in administering this form of treatment, it is possible to extract reliable evidence from many sources with regard to those diseases in which X-rays can be proved to produce definite amelioration or cure.

With the apparatus now at our disposal we can measure the quantity and quality of the rays administered with great accuracy and the same dose can be administered time after time. The main difficulty is the management of the X-ray tube itself, and experience alone teaches the operator to recognise the varying characteristics of the tubes and to select the correct vacuum for the purpose required. It should be laid down as an axiom, therefore, that X-ray treatment should never be undertaken by any other than a medical man with special knowledge of this subject, or an experienced layman acting directly under his directions.

The exact nature of the X-rays is still a matter of conjecture, but their physical and physiological characteristics are well known. It is with the latter entirely that we are concerned in discussing X-ray Therapy.

Their action is certainly very largely local, although lesions outside the sphere of action of the rays in cases where treatment has been administered to one or more areas has been observed to improve. It is suggested that an auto-vaccination occurs and in certain cases this seems to afford the only explanation of the improvement that takes place.

If this is the case the amount of immunity produced is of a weak character, because retrogression is the rule rather than the exception when the treatment is discontinued. The application of the X-rays in small doses gives no sensation to the patient at the time of application, however big the dose, nor is there any visible effect on the skin after the application.

If a full dose is given, after some three to five days an erythema is produced which is evanescent, gives rise to no symptoms, except perhaps a little irritability of the skin, and leaves no traces. If full doses are given repeatedly at intervals bronzing of the skin and desquamation takes place. If more than a full dose is given X-ray burns occur, and according to the dose given different degrees are recognised. These reactions have been divided into three degrees.

The *first degree* consists of reddening and swelling of the skin, with itching which may be almost intolerable, and the symptoms begin ten days to three weeks after the application. The symptoms diminish in from eight to fourteen days and the skin becomes normal except that pigmentation occurs and persists, and later atrophy of the skin with telangiectasis is seen.

The *second degree* begins earlier after the dose, five to eight days, and the formation of blisters followed by crusts takes place. These may take months to heal and atrophic scars appear as soon as the healing is complete.

The *third degree* appears about the third or fourth day—after going through the processes of the second degree perhaps months after the irradiation an ulcer forms in the centre of the region involved. This is accompanied by intense pain, and spontaneous healing seldom if ever takes place.

It is questionable whether it is ever justifiable to proceed even as far as the first degree for therapeutic purposes. The second and third can only be looked upon as fatalities, and are only mentioned to show the extreme danger of want of care in applying this method of treatment.

The *atrophic scars* which occur after a long course of treatment have undoubtedly become in a good many instances the seat of a malignant new growth. It is, therefore, a matter of great moment to the patient that their production should be avoided as far as possible in cases other than those where malignant disease is the disease under treatment.

It is not possible to discuss in detail the different forms of apparatus used to administer

this form of treatment, but it might be well to mention the essentials for a good outfit.

Current—continuous from main or accumulators.
Coil—ten to sixteen inch.
Interrupter—dipper or jet capable of working as low a speed as 180 interruptions per minute.
Valve Tubes and *Spark Gap* } necessary on high voltages to stop inverse current.
Milliamperemeter—which gives the amount of current passing through secondary circuit.
Qualimeter—to give the degree of hardness of the tube.
Tubeholder—with impervious screen and arrangement for inserting aluminium filters and placing pastille to measure dose.
Tubes—with adequate regulating devices to vary the degree of vacuum.

The management of the X-ray tube is a matter of great importance, and on this factor depends very largely the success or failure of the treatment.

Tubes are classed as "soft" or "hard" according to the amount of residual gas in them.

A soft tube offers very little resistance to the passage of the electrical current and gives out rays of low penetration. These rays are particularly irritating to the skin, while on the other hand a hard tube offers great resistance to the current, which is of very high penetration and acts less on the skin. It is obvious, therefore, that the degree of vacuum necessary for any particular case must be carefully chosen and care taken that it is maintained throughout the exposure.

It is found in practice that the "soft rays" are readily absorbed by filters consisting of thin sheets of aluminium felt or leather interposed between the patient and the tube. All tubes have some form of regulating device by means of which the vacuum can be reduced. These are all worked on the principle of letting some gas into the body of the tube, and this is effected either by passing a spark through a secondary chamber containing some material which can store up some reserve gas and release it when heated, or by means of a hollow platinum rod sealed into the tube which will allow osmosis of air into the tube when heated.

It can be seen that though we are able to determine the quantity and quality of the rays at a given moment, the variation which can take place owing to the changes in the vacuum during a given exposure makes it impossible to estimate an exact dose with certainty by the amount of current passing through the tube in a given time.

The method that is generally employed and which is the most reliable is to employ Saboraud's pastilles. These consist of small discs coated with platinocyanide of barium which change colour on exposure to the rays. The pastille is placed halfway between the anode of the tube and the patient, and a standard tint is supplied with which the change in colour of the original disc is compared. When the standard tint is reached the full dose that can be given without the incidence of erythema has been administered. The usual distance employed from the anode of the tube to the skin is fifteen centimetres.

The disc must be looked at from time to time during the exposure. It is found very convenient to have a tachimeter inserted in the circuit. This is a device which records the number of interruptions of the break, and it can be set to cut off the current automatically at any desired number of interruptions.

Where it is noted, for instance, that 10,000 interruptions with the apparatus in use are sufficient to give the full tint, the tachimeter is set for 8000, and when it reaches that number the current cut off, the pastille examined and the tachimeter set for another 1000, and so on till the full dose is reached.

With good tubes it is found that the pastille will reach the standard tint in practically the same time, and it is therefore possible to give a definite proportion of the full dose by reducing the number of interruptions.

Schultz[1] uses 1/3, 2/3, and 3/4, 4/5 and 1/1 doses for skin diseases by estimating the time for full dose and subdividing the time taken accordingly.

He gives the equivalent of one full dose once in three weeks and no further irradiation until three weeks have passed since the completion of the dose.

It is necessary to know the degree of hardness of the tube as accurately as possible.

A rough test is the equivalent sparking distance or alternative path, *i. e.* the distance between the points of the sliding rods of the discharger at which the current prefers to jump the air-gap rather than to pass into the tube. We speak of a tube, for instance, as a five-inch tube when the points of the discharging rods are five inches apart and the current is passing through the tube, and when any approximation of the points causes the current to leap the alternative path—the air-gap. This measurement, however, is not sufficiently accurate, and a better method is to employ some instrument by which we can compare the opacity of two or more bodies of different densities.

[1] *X-Ray Treatment of Skin Diseases*, 1912.

There are several of these and the simplest is Benoist's Radiochronometer. This consists of a disc of aluminium cut away to form twelve sectors arranged in steps of different thicknesses, one to twelve millimetres. The aluminium in the centre is removed and a disc of silver 0·11 millimetre in thickness inserted. This thickness of silver has the peculiar property of being proportionately penetrable by hard or soft rays. The instrument is examined with a fluorescent screen, and according to the hardness of the tube the shadows of the silver and different thicknesses of aluminium correspond. The number of the "step" is then taken to denote the penetration of that tube in the Benoist Scale. There are other instruments by Walter and Wehnelt on the same principle, but the numbers are slightly different.

An improvement on this is Bauer's Qualimeter. This is suspended and attached to the negative pole of the tube and gives continuous direct reading of the penetration quality of the tube during the whole exposure. This is now in general use. The reading is the same as in the Benoist Scale.

The comparison of the different scales in use is given below.

Benoist / Bauer .	1	2	3	4	5	6	7	8	9	10
Wehnelt .	1·5	3	4·5	6	7·5	9	10·5	12	13·5	15
Walter . .	1	1–2	2–3	3–4	4–5	5–6	6–7	7–8		

Speaking generally with regard to X-ray Therapy, the most striking results are obtained in some skin diseases—very small doses being often sufficient to clear up the condition more or less permanently. Where action on the deeper tissues is required there are a good many conditions where marked amelioration takes place, but permanent cure is the exception.

It will be found convenient to discuss the application of the X-rays under two headings—

1. Cases in which the action on the skin alone is required.

2. Cases in which action on deeper tissues is required—Exophthalmic Goitre, Lymphatic and Myelocytic Leukæmia, Lymphadenoma, Fibromyomata, prostatic enlargement and malignant disease.

In considering the treatment of skin diseases, no apology is made for giving in tabular form the technique of Schultz. His technique has been very carefully worked out after a very long experience of X-ray applications.

He divides skin diseases into three groups which from the therapeutic standpoint react similarly.

Group.	Quality of Ray.	Dose.	Interval between Doses.	Cycle.	Resting Period.
I.	7·5 Wehnelt	1/3	7 days	3	21 days
II.	5–7·5 Wehnelt	1/2	14 days	2	21 days
III.	7–7·5 Wehnelt	4/5 1/1	3-4 weeks	1	3–4 weeks

Group I comprises those diseases which are readily improved or cured by small doses.

Under this heading are found many of the varieties of Eczema (nummular, occupation, horny, seborrhœic, perianal and perivulvar), Chronic Suppurative Acrodermatitis, Hebra's Prurigo, Erythema Nodosum, Lichen Ruber Planus, Psoriasis, Chilblains and the eczematous stage of Mycosis Fungoides.

In Group II are found ulcerative, hypertrophic and warty tuberculous conditions of skin and mucous membranes, Bazin's disease or scrofuloderma, fistulous tubercular sinuses and the tumours in mycosis fungoides.

Under the heading of Group III come parasitic diseases of the hair (Sycosis, Favus, Ringworm), Hyperidrosis, some benign tumours of the skin, Keloid, intractable warts and malignant disease of the skin.

In the above lists only those conditions are inserted in which X-ray treatment is employed with a fair chance of success.

Diseases in which this treatment is contraindicated are Acne, Hypertrichosis, Pigmented Nævi, Lupus, Erythematosus, Kerion and Ichthyosis.

Special mention must be made of the treatment of Ringworm. The evolution of this treatment is due to Saboraud, who was responsible for the pioneer work and to whose researches its present success is due.

It has been found that the treatment of isolated patches is not satisfactory, because other patches of diseased hair make their appearance, and it is advisable in nearly all cases to treat the whole hairy scalp.

The rationale of the application is to produce a complete epilation of the whole scalp, and this is effected by giving five exposures of different areas at one sitting. This can be completed with adequate apparatus in one to one and a quarter hours by Adamson's method, which is now usually employed. This dispenses with the old and tiresome practice of screening the rest of the scalp while each patch is treated.

The hair is cut short and five points are marked on the head, one just above and in front of each ear and three in the middle line, one from one to two inches behind the frontal margin of the hair, the second from one to one and a half inches above the flat area of the occiput, and the third just above the lower margin of the hair at the back of the head. The distance

between any of these adjacent points should be five inches. A full Saboraud dose is given with the anode over each of these points and the central regions of each receive a full dose, while the oblique areas receive a correspondingly smaller dose according to the degree of obliquity. This is compensated for by the extra dose received when the neighbouring area is treated, and it has been found that the sum of these doses corresponds to a full dose and complete epilation is the result. The non-hairy parts only require to be shielded from the rays.

The hair begins to fall about the fourteenth day and complete epilation is complete about the twenty-first to the twenty-fifth day. There may be a few roots left, and these must be carefully removed. As a rule the patient is non-infectious in thirty-five days from the application.

In this condition it is absolutely necessary that the correct dose should be applied. A slight overdose to any patch may lead to a permanent complete or partial alopecia of that area, whereas if the dose be just too small only partial epilation takes place, some diseased hair is left and the complete process has to be repeated after a month to six weeks.

Owing to the risks involved, it cannot be too strongly urged that this treatment should only be applied by experts and that no one who has not had the opportunity of studying it carefully at some institution where the proper technique is being successfully used without mishap should attempt to carry it out.

Exophthalmic Goitre.—The results are satisfactory on the whole and the nervous symptoms disappear fairly early, the pulse-rate falls and later the exophthalmos becomes less apparent but does not generally disappear altogether. Treatment should be vigorous up to the production of bronzing of the skin over the thyreoid and continued at progressively longer intervals until the symptoms disappear.

Leukæmia.—X-rays have a marked effect on the blood cells. The leucocytes are reduced and the red cells increased in number. The spleen becomes smaller and the general condition of the patient very much improved. Unfortunately this improvement is not permanent and relapses are certain to occur. Applications should be made over the spleen, the ends of the long bones and the sternum at varying intervals. A blood count should be done fairly frequently and the dosage should be determined by the count and care taken to avoid reduction of the white cells too rapidly.

A full dose can be given to each area and the treatment can be continued until the number of white cells approaches the normal, when rest should be given and the recommencement of the treatment determined on a subsequent definite rise in the number of white cells.

Lymphadenoma.—Very great improvement is apparent after X-ray treatment and life can be prolonged, but in the vast number of cases recrudescence is observed. The glands disappear in a most marvellous way and with great rapidity.

Treatment by full doses filtered through felt or aluminium must be administered and continued until all glands have disappeared and recommenced on noticing any evidence of recrudescence. No other therapeutic agent has given such promising results, and considering the extreme gravity of the prognosis the applications should be persisted in up to the extreme limit of safety as regards the production of an X-ray burn and continued over a period of years.

Fibromyoma of the Uterus.—There is very little literature on the treatment of this condition in England, but a very large number of cases have been treated by various Continental radiologists and their results have been very satisfactory on the whole.

The rationale of the treatment is that an artificial menopause is produced by the action of the X-rays on the ovary, while at the same time there is a certain amount of direct action on the tumour itself.

Bordier [1] in his paper read at the Electro-therapeutic Section of The Royal Society of Medicine gives the indications and contra-indications for employing radiotherapy. He lays down that the patient should not be less than thirty-nine years of age and states that the cases that give the best results are interstitial fibromyomata, where hæmorrhage is the chief feature and where the tumour is not excessive in size.

He gives a series of irradiations consisting of three cycles, one over the central and one over each lateral region, nine in all on nine successive days with an interval of from twenty to twenty-five days between each series, and finds that from three to four series are sufficient to produce the required effect.

Albers-Schönberg [2] in his last paper on this subject states that in properly chosen cases he has obtained 78 per cent. of cures. He uses two tubes working at the same time, one above and the other below the patient, and gives in each series four sittings of eight minutes each, making in all between $60x$ and $100x$ on Kienbock's scale (this corresponds to 30H–50H units). He recommends that the following types of cases should not be treated by X-rays: pedunculated myomata of the neck of the

[1] *Archives of Röntgen Ray*, No. 146, 1912.

[2] *Archives d'Électricité médicale*, April 10 and 25, 1913.

uterus and all cases where there is any possibility of the added presence of malignant disease, and those where acute retention has been caused by pressure on the bladder. He uses filters of aluminium two millimetres in thickness and advocates the use of a compressed diaphragm.

Hænish [1] gives results of treatment of fifty cases of which 50 per cent. were cured.

All radiologists are agreed on the necessity of using high tubes (8–9 Benoist) which must be capable of keeping up their vacuum during the whole exposure.

Hypertrophy of the Prostate.—Good results have been obtained from irradiation with hard rays. The cases which are most suitable are those where the hypertrophy is not excessive or of very long standing. A series of six séances with a tube of 7–8B. applied through the perineum through a felt filter at intervals of three or four days is recommended, and if improvement takes places in the symptoms after this procedure it is advisable to continue the treatment.

The first effect is to lessen the frequency of micturition and improvement in the flow, and subsequently the urine becomes clear owing to the non-retention of residual urine.

X-rays in Malignant Diseases.—With the exception of Rodent Ulcer the results of treatment of malignant disease is in the main disappointing, although very marked improvement in the symptoms and the local conditions are often obtained and maintained for a considerable period. This may be said, however, that there is no other therapeutic agent but irradiation with X-rays or radium that has such inhibitory action on the cancer cell, and that improvements in the method of application may produce more lasting effects. There seems to be no doubt that the X-rays have a definite selective action on embryonic cells. This is shown very clearly by their destructive action on the cells of the ovary and the testis; but there is another view put forward, that the beneficial action is due to a stimulation of the healthy cells to resist the action of the diseased cells. The difficulty that has to be faced at the outset is to overcome the absorption of the therapeutic rays by the superficial tissues of the body and to obtain the required action on the deeper structures without damage to the superficial parts. If the theory that the action is due to some antitoxin produced in the body is correct, it might be feasible to irradiate different parts of the body with large doses and so avoid any damage to the skin, but the general belief still holds that the action is almost entirely local. It is a common experience to find a local recurrence healing under the influence of X-rays while secondary deposits are forming elsewhere and the patient is steadily becoming worse.

[1] *Brit. Med. Journal*, October 1912.

Under no circumstances should X-rays be employed to the exclusion of operation where operation is possible. Pre-operative irradiation is universally admitted to be unjustifiable.

Treatment should be vigorous and prolonged. Small doses of X-rays at long intervals undoubtedly stimulate the growth of the cancer cell and therefore should never be employed. The older method was to give small doses frequently, and good results were obtained only owing to the frequency of application, the action being cumulative. Since the use of filters has become general it is possible to administer very large doses without any fear of severe damage to the skin. The applications should be given over a wide area beyond the primary focus and continued with periods of rest for a prolonged period. In a hopelessly inoperable case it is justifiable to give extremely large doses, and it has been demonstrated that marked amelioration has been produced, although a cure has not been effected.

In rodent ulcer in the early stage the result of X-ray treatment is very satisfactory, but where cartilage or bone is involved it is better to resort to surgical measures at once, because it is very rare to find that complete healing takes place under X-ray treatment and valuable time is lost because the growth may spread into the deeper tissues and make the task of the surgeon more difficult to completely eradicate the growth. In the early stages sound healing of the ulcer may be obtained by the use of radium, carbon dioxide snow, or ionisation with zinc. Experience of over twelve years, however, shows that recurrence even after many years is the rule rather than the exception, and patients should be advised to keep under observation from time to time and to report at once if any sign of recurrence takes place.

Primary Epitheliomata and Epitheliomatous glands are very little affected by the X-rays, and in some cases have been observed to spread very rapidly after irradiation. It is practically useless to employ this form of treatment. Where enlarged glands in the neck appearing after an operation for epithelioma of the tongue have been noticed to subside they were probably only inflammatory.

Sarcomata sometimes respond to X-ray treatment in the most marvellous manner, complete disappearance of very rapidly growing tumours taking place, but recurrences and metastases nearly always occur. Instances of prolonged arrest of the growths have been reported. It is worth while to treat all inoperable cases, however, because apparent cures up to several years have been known to occur.

Carcinomata.—The situation in which this is found most amenable to treatment is carcinoma of the breast.

Here one may have to deal with a primary growth which has become inoperable before it has been brought to the observation of the medical man, or where the patient absolutely refuses operation when feasible.

In all except the rapidly growing type of case great improvement takes place, the growth becoming smaller and apparently remaining localised. Such patients may continue for years in good health and without pain.

The second type of case is that in which an operation has been performed and recurrence has taken place in the skin or glands with or without the formation of nodules or ulcers accompanied by pain.

Here the results of treatment are most satisfactory for more or less prolonged periods. The nodules disappear, the ulcers become clean and granulate and heal, and the pain is alleviated or stopped. By the time, however, that the above signs and symptoms have manifested themselves, it is almost certain that the disease has affected the deeper tissues, and in spite of the local improvement, extension to the mediastinum, lungs and pleura and metastatic deposits in the bones manifest themselves and cause death.

When we consider the fact that the X-rays have the power to cause the complete disappearance of the cancerous nodules in the skin, it seems only reasonable that early prophylactic treatment after operation is a logical course to pursue. These recurrences must be due to the unavoidable release of some cancer cells into the wound at the time of the operation, and the sooner after the operation that the X-rays can be brought into play to influence these stray cells, the better chance there must be of killing them. It is difficult to prove that this prophylactic treatment is effective, because it is not possible to say in any particular case that these cells have escaped, but a routine course is recommended by many surgeons after any operation where the growth though operable was extensive.

The treatment should be thorough, and the whole of the affected side back and front should be subjected to a series of irradiations, and this should be continued at lengthening intervals for at least a year after the operation.

Sir J. J. Thomson discovered that certain metals give off secondary X-radiations when the rays from an X-ray tube were allowed to fall on them. He found that this radiation is specific for each metal in penetrative power and is the same whatever the quality of the incident ray—silver unit rays being identical with the β-radiation of radium. Hernaman Johnson [1] has made use of this fact, and in cases of partial obstruction of the bowel by malignant disease has administered a fairly large dose of precipitated silver in a meal, and when this has arrived at the required spot (determined by the fluorescent screen), he gives an exposure over the affected region with a hard tube with the object of getting the secondary X-radiation to act at the site of disease. This dose is repeated at intervals and good results as far as symptoms are concerned have been obtained.

In a subsequent paper [2] he discusses secondary X-radiation at greater length and describes his X-ray transformer, in which the patient is screened from the radiation of the tube itself and is only affected by the secondary radiation from the plate of metal on to which the rays impinge. Although the results of treatment by these secondary radiations have not been very striking as regards permanent therapeutic results, enough has been done to make it evident that this method is worthy of further study.

A. D. R.

ELECTROTHERAPEUTICS

There is, perhaps, no therapeutic agent that is so potent for suggestion or so dramatic in its manifestations as electricity. It is, therefore, little wonder that it has been, and is, still exploited by charlatans, with the result that an extremely valuable agency fell into disrepute. Fortunately, however, this phase has passed and the public no longer looks askance at a medical man who employs electricity in the healing art.

The application of electricity to medicine is a subject that involves a certain elementary knowledge of the physical laws involved, and many medical men who "dabble" with electricity fail because they do not possess this: they buy a battery of some kind and expect to work wonders by turning on a switch. Failure naturally results, and they lose faith in the method, whereas their lack of success is often simply because they have not applied their resources efficiently. It is a study that will repay medical men in almost every branch of the profession. Success in the treatment of disease by electricity depends on the efficiency of the apparatus and the technique, but the personal equation cannot be overlooked, and no physician is likely to be successful unless he can inspire his patient with confidence both in himself and in the method he employs.

In the space at our disposal we do not propose to enter into the physical details of electricity, which may be obtained from any of

[1] *Archives of Röntgen Ray*, December 1911.

[2] *Trans. Royal Society of Medicine*, Electrotherapeutical Section, 1912.

the large number of elementary textbooks, nor can we deal at length with the various forms of electrical treatment that involve expensive apparatus, such as the high-frequency and static current. Our purpose is rather to give an outline of the various applications of electricity that a general practitioner, with comparatively simple and cheap apparatus, may himself undertake efficiently.

We have already referred to the suggestive factor in the applications of electricity, and doubtless this may be turned to advantage in certain cases. Elaborate and complicated apparatus has certainly an advantage in this respect, but the average medical practitioner cannot afford such luxury. But, apart from this factor, it is surprising what elasticity a simple galvano-faradic board will give to the man of ingenuity and resource. By various home-made devices with metronomes, clock-work, etc., he can produce most of the effects that the more complicated sets of apparatus will give for stimulating muscular contractions or helping the circulation, and practically all the electrodes required for ionisation may be made by himself to suit the particular needs of each case.

The Galvanic Current.—The ordinary continuous current is the most important in electric treatment; for, although its use is mainly for ionisation, it can be transformed and altered in various ways to give quite a variety of effects. It is derived from batteries of dry cells, from accumulators, or from the town's mains, the first of these being the best for ordinary work. In using the mains a resistance-board must be interposed to reduce the voltage to such limits as are applicable in medicine, *i. e.* from 0 up to 50 or 60 volts. Some form of rheostat to increase the current gradually so that the patient does not receive shocks is also necessary, but this presents no great difficulty.

Various modifications of the constant current are in general use. The simplest is the interrupted continuous current, the interruptions being made either by hand or by an instrument designed for the purpose, such as an ordinary metronome that is adapted in such a manner that it forms a contact at each beat by dipping a wire into a cup of mercury. The effect of this is to give a series of shocks of a more or less painful character (diagrammatically represented thus: ⊓ ⊓ ⊓ ⊓). These are useful for producing contractions in wasted muscles. A better form of this current, and one that is not painful, is produced by sliding the rheostat (the resistance which controls the strength of the current), either by hand or mechanically, so that the current is gradually increased and diminished in intensity. The employment of this current will be found very useful in the treatment of paralysis and various other conditions in which stimulation of muscles is required. The *sinusoidal* or alternating current is another modification of the galvanic current, and is produced by means of a motor transformer. It is, perhaps, the most useful variation that we have for purposes of stimulation. It is represented diagrammatically thus: ∿∿∿∿∿∿ The rate at which the alternations of the current occur is regulated by the speed of the motor (anything from 100 to 3000 per minute), and the best results are obtained by the slower rather than by the more rapidly changing currents.

The great feature is that although the potential is always changing there are no shocks because the voltage is always rising and falling *gradually*.

The **Faradic Current** has been replaced to a great extent by the sinusoidal, but for certain purposes it is of value. A special coil is required, and it should be noted that some of those that are sold for medical work are almost useless as they are altogether too small; the currents that are given out from them are not only too feeble to be effective but also very painful to the patient. Even with fairly large coils, however, the faradic current is much more painful in proportion to the quantity of current passing through the patient than any of the other forms.

The **Static** and **High-Frequency Currents** both require costly and elaborate apparatus and are hardly ever applicable to general practice. But it often happens that these forms of treatment are available in institutions where a general practitioner is in charge, and it is with a view to his guidance that we include these brief notes.

The high-frequency current, commonly known as H.F., is one of great potential and is capable of producing big sparks which are quite harmless owing to the small quantity of current that is passing and the extraordinary rapid oscillations that occur (millions per second). It is the most dramatic and sensational form of current we have, and consequently it has been more exploited by charlatans than any other. Naturally medical men look askance at any form of treatment that is so abused, but, in spite of the haphazard and unscientific methods of many of the institutions that flourish on the credulity of a gullible public, the fact remains that many patients receive great benefit there. It is very much to be regretted that this valuable form of treatment should have got into such hands and have attained notoriety, but that is no reason why medical men should despise it, for we know of no other form of treatment that is so

successful in treating cases that are dependent on vascular tension. The manner in which the current acts is not known, but the later types of apparatus are extremely effective, and are capable of raising the body temperature several degrees, and it is believed by some workers that the thermic effect is the key to its action.

The chief methods of use are (1) condensation, (2) sparking, (3) thermic effects (diathermy).

1. *Condensation* is carried out by placing the patient on a couch that is covered with metal from which he is separated by a mattress. He holds a metal handle that is connected with the top of the instrument, and when the apparatus is working sparks can be drawn from him. The patient experiences no definite sensations, but the treatment has a soothing effect and a general feeling of well-being is produced. This treatment is of service in various ill-defined conditions that may be classed under debility, and it has a pronounced action upon the blood pressure.

2. *Sparking* may be applied directly by means of a metal point, but is more usually applied through vacuum electrodes made of glass; the current from the machine flows into the electrode and induces a current on the outer surface which sparks on to the skin when the electrode is brought near. The method of sparking with glass electrodes has been used for various forms of skin diseases, such as chronic eczema and psoriasis, with fairly good results, but the X-rays and other forms of treatment have replaced it in this field, while CO_2 has taken its place in dealing with nævi.

The direct sparking by means of a metal point is called fulguration, and powerful sparking from H.F. machines has been used in the treatment of inoperable cancers with a certain amount of success, especially when combined with operative procedure as extensive as the nature of the disease permitted.

This method has also been applied to port-wine marks; but although there is a certain amount of improvement it is hardly commensurate with the time and patience necessary in carrying out the treatment.

3. *Diathermy.*—By means of certain modifications in the most recent and powerful H.F. machines it is possible to produce very marked thermic effects. The current may be applied to any part of the body and the temperature raised by several degrees, in fact the albumen can easily be coagulated. The treatment has been applied to various joint affections and other conditions, but as yet the experience of this new therapeutic procedure is limited in this country. This current may also be used locally for surgical purposes and it is probable that it will supersede the knife for the removal of vascular tissues, because as the instrument passes through it seals the vessels with blood coagulated by the heat and prevents all bleeding.

The **Static Current** is a form of electricity that is much used in America and requires elaborate and expensive apparatus. It has not found favour in England, partly no doubt on account of the technical difficulty in producing these currents in a damp climate. The feature of this form of electricity is that the pressure (voltage) is exceedingly high, but the quantity of current (amperage) is low. The instruments produce a current absolutely in one direction that may be used for actuating an X-ray tube; in fact, this form of generator was in common use for this purpose in America at one time. The voltage is so high that sparks of six or eight inches may be produced, but the quantity of current is so small (about one milliampere) that no ill-effects are experienced by receiving a shock of such apparent magnitude.

When the machine is charged and the current cannot spark across a gap it diffuses itself in the air in a brush discharge that gives a crackling sound and electrifies all objects in its neighbourhood. By connecting the patient to one pole and placing him on an insulated stool beneath an electrode connected with the other pole, the patient is "electrified," and sparks may be drawn from him by any person standing on the floor. The "condensation couch" used for H.F. applications may also be employed in conjunction with this machine.

This form of treatment is said to have a very soothing effect and has been used in sleeplessness with some success.

The sparks from the static machine have also been used by some workers for direct sparking, but the high-frequency current is better for this purpose.

Methods of Application

The galvanic, faradic, sinusoidal and all similar currents may be applied locally, by means of suitable electrodes, or generally, the patient being placed in a bath of some kind. The full bath has fallen out of use, as it is impossible to estimate what proportion of the current passes through the patient, and it has been replaced by the four-cell bath of Dr. Schnee, which has found universal favour. Separate earthenware vessels are supplied for each of the extremities, and in each of these baths a carbon electrode is placed. The current can be passed in any direction through the patient as desired, and can be exactly measured.

A word of warning must be given. If the town's mains are utilised for supplying current to baths or instruments, the greatest care must be taken that no water-pipes, gas-taps, electric-fittings or other metal-work connected with the earth are within reach. Very severe, even

fatal, shocks may be received by patients touching such objects when they are in the bath or holding one of the instruments.

Electrodes are the applicators through which the current reaches the patient. Various types are in general use, the most usual being made of metal covered with layers of lint or chamois leather. The most important point is that there should be good contact with the skin, but care must be taken that no part of the exposed metal is allowed to touch the patient, otherwise a burn will be produced by the excessive electrolysis that will take place at this point. For electric massage metal rollers, covered with lint, are employed.

In all cases the circuit through the patient must be completed, and for this purpose a large indifferent electrode is placed on some convenient part of the body. It is most important that this indifferent electrode should be of sufficient size when big currents are used or a burn will result. A feeling of burning will precede the formation of a burn, and this must be borne in mind when patients speak of any pain during an application. In our own work we use pieces of copper gauze of suitable sizes and cover them with two or three layers of gamgee tissue. Instead of employing an electrode, however, when large currents are to be used, it is better to place one of the limbs in a vessel containing a weak saline solution and to make this the return circuit.

Ionic Medication.—When two wires from a galvanic battery, or from any other source of constant (unidirectional) current, are placed in water, electrolysis takes place and the water is separated into its elementary constituents; the hydrogen is given off from the wire connected with the negative pole, the oxygen from that connected with the positive pole. If common salt or any other soluble salt is dissolved in the water, it also is split up into its component molecules, the basic radicle (the sodium) is given off at the positive pole while the acid radicle (the chlorine) is liberated from the negative terminal. If the copper wires are placed one above and one below a pile of damped sheets of blotting paper and the current is allowed to flow through them, it is found that copper can be detected in the blotting paper near the positive pole and penetrating many layers of it towards the negative pole, but that no copper has passed into the blotting paper near the other wire. In the same way the copper could be made to penetrate into the body from a copper electrode placed in contact with the skin. For practical purposes, however, it is not usual to employ the metal directly in contact with the surface, but to interpose some layers of lint soaked in a 2 to 4 per cent. solution of one of the salts of the metal we wish to use, and to place behind it an electrode made of the same metal connected with the positive pole. In exactly the same manner we can drive in acid radicles such as salicylate of soda by connecting with the negative pole a pad soaked in a solution of this salt. The circuit is completed by means of a *large* indifferent pad electrode placed in some convenient situation or by immersing a limb in a bath containing an ordinary carbon electrode.

This method is not limited to the treatment of small areas. A knee can be enveloped in a large pad from which the ions may be driven into the joint or the drug may be forced through a larger area by immersing the legs or arms in baths in which the drugs are dissolved.

The following table shows the most commonly used drugs and the electrode which must be employed—

+ *Driven in from the Positive Pole.*	− *Driven in from the Negative Pole.*
Sodium	Chloride
Potassium	Iodide
Lithium	Sulphate
Sodium	Salicylate
Zinc	Sulphate
Magnesium	Sulphate
Cocaine	Hydrochloride
Copper	Sulphate
i. e. The ions of all metals, etc., and basic radicles, such as NH_4.	*i. e.* All acid radicles.

For ordinary ionic medication a battery that is capable of giving 40 volts is amply sufficient. The quantity of current used varies with the size of the area under treatment and the individual susceptibility of the patient. For small areas it is found that patients will not tolerate more than a few milli-amperes. The minimum current that will be of value is about 3 ma. per sq. cm. for 12 in.; in the treatment of large surfaces, such as a knee-joint, 40 or 50 ma. are easily tolerated by the majority of patients, and in exceptional cases as much as 120 ma. may be given.

Twenty minutes is an average dose, but naturally the length of time needed for each application varies. In ionic medication the greater the current borne by the patient, the deeper will the ions penetrate, hence in some cases it is better to give one big dose, with an anæsthetic, than multiple doses of comparatively small intensity at frequent intervals. Under the influence of an anæsthetic, ionisation can be used to great advantage, for there is practically no limit to the quantity of current that may be passed, provided that no shocks are given. In the treatment of rodent ulcers and small new growths where excision is not indicated this is of great importance, for the

whole treatment may be effectively accomplished at one sitting. A bare zinc electrode is held in firm contact against the surface until the grey appearance extends to one-eighth of an inch, and if the edges are at all heaped up zinc needles are thrust into them until the whole of the affected area has been treated. Healing takes place fairly rapidly and there is seldom any pain. Collodion dressing is all that is necessary and there seems to be very little tendency for these cases to become septic.

The question may be asked, why, if an anæsthetic is necessary, should the ulcer not be excised? The cosmetic effect of ionisation in this way is much superior. There is practically no scarring and there is no tendency to contraction, so that in all operations on the face this should be the method of choice. Moreover, in reasonably early cases a certain cure may be relied upon in practically every instance. Recurrences are seen in all forms of treatment of rodent ulcer, including excision, and so far as our information goes the chances of recurrence with thorough ionisation are rather less than with other forms of treatment.

Electricity in one or other of the above forms has been applied beneficially to a great number of diseases differing widely in their character. The list fortunately includes some affections which are very obstinate in their reaction to other methods of treatment. It is necessary, however, to protest against the indiscriminate use of electricity, especially in the hands of unqualified persons, when experience has shown that there is little or no prospect of any benefit resulting from its use.

In addition to the effects produced by electrical applications upon the local conditions for which the treatment is adopted, their general tonic action must be emphasised, as this is undoubtedly of great therapeutic value in all cases. The appetite and general condition are improved, the patient sleeps better, and in many cases constipation is relieved. The circulation is stimulated, and we are of opinion that when the two- or four-cell bath is used for rheumatoid arthritis, or other lesions, much of the improvement that results is due to the improved circulation through the affected part.

We have included in the following list those diseases in which in our experience electrical treatment has given encouraging results, or in which the published records appear to merit notice.

Anæmia (Chlorosis).—Some form of general electrisation may be usefully combined with other medical treatment, and considerable benefit may often be obtained from the general tonic action referred to above, especially when the sinusoidal current is applied by means of the four-celled bath. Those who have employed H.F. speak well of the results they obtain by the use of the condensation couch.

Anæsthesia (Local).—Local anæsthesia may be induced by the ionisation of cocaine from the positive pole, a 2 per cent. solution being used. The method may be very conveniently employed as a preliminary to the removal of hairs by means of electrolysis.

Arterio-sclerosis.—In this as in other conditions associated with high blood pressure the H.F. condensation couch gives very good results; even a single sitting often produces a marked fall in the pressure. The elimination of waste products by the urine is also increased and the treatment, therefore, may be beneficial in granular kidney.

Carbuncle.—Zinc ionisation, by means of a zinc needle passed into the centre of the carbuncle, not only relieves pain but frequently effects a rapid cure. In bad cases more than one application may be necessary.

Carcinoma.—Zinc ionisation has also been tried in carcinoma; zinc needles are run into the growth and a large current is used. The sloughing of the growth which results is followed by a comparatively healthy ulcer, and healing may then be encouraged by further ionisation through lint pads soaked in a 4 per cent. solution of zinc sulphate (positive pole). Fulguraction by means of H.F. sparking has also been recommended. [For *Diathermy* see separate article.]

Cardio-vascular Affections.—The action of the H.F. condensation treatment in reducing high blood pressure has already been noted. A peculiarity about this method of treatment is that it is equally valuable in producing the opposite effect when the tension is too low, the tendency in both cases, therefore, being to restore the pressure to the normal. (The Bergonié treatment described under *Obesity* is also an important agent in certain forms of heart disease.)

Chilblains.—The constant and sinusoidal currents used with the four-cell bath for half an hour twice or thrice a week brings about considerable improvement, and in some cases actually cures the patient. Half a dozen to a dozen baths usually effect a marked improvement in the chilblains, and in many cases we have found the cure a permanent one. The general health is also much improved, and the patients invariably find that they suffer less from cold extremities in severe weather, even after having only three or four baths.

Constipation and Atony of the Digestive Tract. Nearly all patients when treated with the sinusoidal current for a variety of conditions volunteer the statement that they note a

distinct improvement in the action of the bowels when there is any tendency to constipation. It is most marked when a current of slow periodicity is employed, but it is uncertain whether this is due to the general tonic action and the strengthening of the abdominal muscles or to the direct stimulation of the peristaltic movements of the intestines. Constipation is, roughly speaking, of two types, *i. e.* due to atony of some part or parts of the colon, or to inefficient defæcation. In the former type the best plan is to apply the current by means of pads over the course of the colon or to place a large pad on the back and apply the sinusoidal current by means of a roller electrode to the abdomen, the result being a combination of electrical treatment and massage that is very effective. When, however, the trouble is inefficient defæcation, it is best to apply one pole actually in the rectum with a special rectal electrode, the other electrode being placed on the abdominal wall. The three-phase current is also useful for this class of treatment.

Debility. — The general tonic effect of the four-cell bath, to which attention has already been drawn, is a most valuable therapeutic agent in the treatment of debility arising from overwork, or as the result of influenza, etc. The four-cell bath, using both the constant and sinusoidal currents, is our routine practice for these cases, and, although it is perhaps rather slow and tedious, the results are quite worth the time expended and it is very seldom that the patients relapse. Other workers speak of the results of auto-condensation with the H.F. current with enthusiasm, but our preference is for the four-cell bath.

Diabetes. — In simple glycosuria the H.F. condensation is said rapidly to bring about a complete disappearance of the sugar from the urine. In true diabetes mellitus the treatment does not seem to be of any use.

Dupuytren's Contraction.—See *Keloid.*

Exophthalmic Goitre. — The faradic current has been used largely in the treatment of this disease, and also the ionisation of the gland with potassium iodide (negative pole). But it seems likely that all other forms of treatment will give place to X-ray therapy, as this is in our experience the only reliable means of obtaining improvement.

Fistulæ.—Good results may be obtained from the ionisation of fistulæ and sinuses of all kinds with zinc, provided that they are not due to the presence of a sequestrum or other operable cause.

Gout.—Gouty arthritis may be treated as other forms of chronic arthritis by means of the two- or four-celled bath, and we believe that the effect of the electricity alone is as successful as when salts are introduced by cataphoresis. In acute cases the anode should be applied to the painful joint or joints, and when the subacute stage is reached a mild sinusoidal current may also be used. If preferred, lithium sulphate or carbonate may be placed in the tub or tubs connected with the positive pole.

In the absence of acute joint lesions, gouty patients may be treated upon the H.F. condensation couch in order to increase the metabolic changes; that this actually takes place is demonstrated by the increased output of urea.

Gynæcological Conditions. — *Amenorrhœa.* — When amenorrhœa is caused by anæmia or debility good results may sometimes be obtained from one of the methods of general electrisation. We prefer the galvanic and sinusoidal currents applied through the four-cell bath, or the H.F. condensation couch may be employed.

Vaginitis.—A specially constructed electrode is employed which allows the vagina to be distended with a 2 per cent. solution of zinc sulphate (positive pole). The treatment is usually very successful.

Chronic Endometritis.—The uterus may be ionised for this complaint by means of a specially constructed copper or zinc electrode, connected with the positive pole; the electrode is insulated to within two inches of the end, and is passed into the cavity of the uterus. A current of from 10 to 12 ma. should be used for about 15 minutes. When using a copper electrode care must be taken at the close of the treatment to pass the current in the reverse direction for two or three minutes before attempting to remove the instrument, since it tends to adhere firmly to the cervical canal as the result of the electrolysis. For this reason a zinc electrode is preferable and the results are quite as good with this metal as with copper.

The effect of this method of treatment is usually as successful as that of curetting. A course of from six to twelve treatments is necessary.

Dsymenorrhœa and Menorrhagia may be treated in the same manner; in the latter complaint the hæmorrhage usually ceases after two or three ionisations.

Hæmorrhoids.—In slight cases of hæmorrhoids we have had good results from the use of the vacuum electrode connected with the H.F. machine, but in severe or longstanding cases the treatment is quite useless. We have also had success by means of ionisation with zinc needles.

Headache. — When caused by overwork or general debility, headaches may often be greatly relieved by the faradic current applied to the back and front of the head through large pads. A large faradic coil must be used, as the currents from the small instruments are too painful.

Incontinence of Urine.—Incontinence in children may be treated by means of a pad placed over the perineum, the other electrode being applied to the lumbar vertebræ. In adult females the sphincter may be directly stimulated by a bougie electrode introduced into the urethra. The bladder being full an attempt is made to produce a desire to micturate, and in some cases one form of current appears to be more efficacious than another. We frequently use a combination of the faradic, interrupted continuous and sinusoidal currents, and in many cases we have been very successful. The best results are obtainable in the cases which are a persistence of the nocturnal incontinence of infancy, while some others appear to be unaffected by the treatment. If there is mental deficiency, there is little hope of benefit.

Insomnia. — Electricity certainly cannot be claimed as a specific for insomnia, but in some cases relief may be obtained from the use of the faradic current, applied to the head as in the treatment of headache. Static electricity and the H.F. couch have also been recommended, but we have not found the results very encouraging.

Keloids and Dupuytren's Contractions. — The ionisation of these conditions by chlorine ions (sodium chloride, negative pole), usually gives good results; large currents, up to 60 or 80 ma., must be used, and the treatment must be carried out thoroughly. We ourselves prefer to treat keloids with the X-rays.

Locomotor Ataxy.—Faradism of the spine has been much used in the treatment of locomotor ataxy, and certainly appears to relieve some of the symptoms. We have not, however, observed much improvement from the use of this or any other form of electrical treatment.

Lupus Vulgaris. — Ionisation must now be considered as one of the alternatives to the Finsen and X-ray methods of treatment for lupus, and it offers a very good hope of success. When the surface is ulcerated, direct ionisation with a 4 per cent. solution of zinc sulphate on a pad (positive pole) may be carried out; if, however, the surface is not broken it should be first painted with sodium hydrate, and the thick cuticle scraped off before the treatment is commenced. In some cases the apple-jelly nodules prove very resistant, and they may then be removed by the zinc needle inserted into the centre of each nodule.

The cosmetic result of ionisation in lupus is very satisfactory; it compares favourably with that of the Finsen light, and is far superior to the average X-ray result, as there is no danger of the formation of telangiectases.

Mucous Colitis and Ulcerative Colitis. — There are few diseases in which the medical treatment is less satisfactory yet with ionisation this class of case yields very satisfactory results in the majority of instances, although a certain number fail to react to treatment of any kind. Of course before resorting to ionisation or any other form of treatment, all possible sources of septic absorption must be carefully sought out and a rigid treatment of all suspicious teeth insisted on, not forgetting that bridges that look excellent may harbour decaying food debris that cannot be cleared out.

The treatment consists of ionisation with zinc or copper into the large intestine from a solution of one of the salts. The current chooses the paths of least resistance and carries with it the ions that we wish to introduce. We employ zinc sulphate solution (4 per cent. positive pole), and inject one and a half pints, a quantity that is ample for irrigation of the whole of the large bowel. Smaller quantities should be used at first until it is found that the patient will tolerate this quantity. A special rectal electrode should be made—a piece of zinc rod with a hole through is what we employ, and in order to avoid the electrolysis that would occur at the sphincter, we insert it in a rubber finger-stall with a few holes cut in the tip. This electrode is coupled with a rubber tube to an ordinary douche-can, while contact is made through a wire soldered to the electrode. A large indifferent electrode is placed behind the patient's back so that he lies on it. When only the lower part of the bowel is affected the patient is propped up, but for treating the whole large intestine he lies flat.

The quantity of current employed varies greatly and patients can stand as much as 150 ma. without any real pain, but a very emphatic warning must be given against using too large a current, as will be explained later. We do not, as a rule, exceed 50 or 60 ma., our practice being to find how much the patient can stand quite comfortably, and then to continue the treatment with about half that quantity. The current is turned on as the liquid flows into the bowel and a careful watch is kept on the milliampere-meter, and also on the patient's pulse, remembering that these patients are usually nervous and that it is as well to begin with small doses rather than with large until we know what the patient will stand. This is a most important point, because some patients experience a very serious degree of shock after the treatment, of which there is no warning at the time. It comes on about five minutes after the current is turned off, the patient suddenly showing signs of collapse, with cold clammy sweat, vomiting and a weak thready pulse. It does not occur in all cases, perhaps in half, and we have seen it in both men and women. We do not know what

the cause is, but it can be avoided to some extent by giving an injection of morphia beforehand, using only small currents, and turning the current off very slowly. The treatment is on the ordinary lines adopted for shock, and our experience is that it passes off in a quarter to half an hour.

The treatment is continued for about ten minutes at first and lengthened out as tolerance is established. The tendency to shock becomes less marked as the treatment continues, and in some cases no shock is noted at all after the first two or three doses. Treatment is given twice a week at first, but afterwards only one dose a week is necessary. The bowel is voided of the solution as soon as the treatment is over.

The results of ionisation are certainly very satisfactory, provided the patient will tolerate the shock that occurs in such a large number of cases. Forewarned is forearmed, and if the patients know what to expect they are much more likely to persist in a treatment that gives a better chance of success than any other of which we have experience, including irrigation through an appendicostomy.

Muscular Rheumatism. — The constant and sinusoidal currents, applied to the affected muscles either through the two- or four-cell bath, or still more beneficially by means of the roller electrode, brings about a rapid improvement. During the acute stage only the constant current with the anode connected to the painful part should be employed, but in chronic cases we have found the sinusoidal current of great use.

Nævi. — Since the introduction of carbonic acid snow electrolysis is less frequently employed in the treatment of nævi. We still find it of use, however, for the purpose of finishing off any small areas remaining after the carbon dioxide treatment. The electrolysis is carried out by means of a platinum needle, connected with the negative pole, thrust through the nævoid tissue. If the nævus is large, several needles connected alternately with the positive and negative poles and held in a special holder are employed, but of course this needs the assistance of an anæsthetic.

Capillary nævi, or port-wine marks, may also be treated in the same way with a very fine needle, but the treatment is very tedious and leaves a certain amount of scarring. We have also obtained some improvement in these cases by H.F. sparking from a vacuum electrode under an anæsthetic, but as yet there is no really satisfactory treatment for these cases, although both these methods bring about a certain amount of improvement.

Obesity.—The only form of electric treatment which appears to give satisfactory results in obesity is that afforded by the Bergonié apparatus. The outfit is a costly one, but the claims made on its behalf seem to be correspondingly strong. The apparatus consists essentially of an induction transformer designed to produce the "maximum of muscular contraction with the minimum of sensation"; the rate of interruption is capable of great modification, and is regulated by means of a metronome. The current is applied to the limbs through brass electrodes which are fitted in close contact with the skin.

We have no personal experience of this form of treatment, but according to the published results it produces a steady decrease in weight, accompanied by an improvement in the general health.

Papillomata and Warts. — The effect of the ionisation of warts with magnesium sulphate is very striking, the warts disappearing in the course of some three or four weeks after a single treatment. When the epithelium covering the warts is very dense it is advisable to prick it with a needle before ionisation is begun. The ions may be driven in through a pad soaked with the sulphate and connected with the positive pole, or the whole hand may be immersed in an arm bath containing a solution of the salt, after first pricking all the warts with a needle.

Paralysis.—During the acute stages of neuritis nothing more than a mild constant current should be used, but in the absence of acute symptoms the paralysed muscles may with advantage be treated with either the faradic or sinusoidal currents; these should be applied directly to the affected muscles through a pad or roller electrode.

Pruritus of the Anus or Vulva.—These conditions can nearly always be relieved by mild sparking from the H.F. vacuum electrode. We have also obtained very good results with X-ray treatment.

Rheumatoid Arthritis. — Electricity is a very valuable therapeutic agent in rheumatoid arthritis. When a single joint is affected the current may be applied locally by means of pads shaped to the part, or through the two- or four-cell bath when many joints are involved. A combination of the galvanic and sinusoidal currents may be used, or ionisation may be employed; in the latter case the pads are soaked in a solution of iodide or salicylate of soda and connected with the negative pole, or the salt may be dissolved in the water used for the baths. The theory is that the galvanic current sets up ionic changes in all the tissues through which it passes, while the effect of the sinusoidal current is to cause fibrillary muscular contractions which promote the circulation and help in removing the waste products that have been

liberated by means of the ionisation. But we believe that the improvement is due chiefly to the improved circulation.

It should be noted that in the majority of cases the first few treatments bring about no amelioration in the symptoms, and may actually make the condition temporarily worse, but these are the cases which usually give the best results in the end.

Rodent Ulcer.—During recent years X-rays, radium, carbon dioxide snow and ionisation have been introduced as alternatives to excision, and in reasonably early cases they are all very successful methods of treatment. They all have the disadvantage, however, of being comparatively useless when bone or cartilage is involved.

The advantages of ionisation over the other methods enumerated are the simplicity and ease with which it may be performed, and the precision with which the disease may be attacked. It is therefore by far the best method to adopt when the disease is in a difficult position to treat, such as the margin of the eyelid. The treatment is carried out by placing several layers of lint soaked in a 2 per cent. solution of zinc sulphate over the ulcer; a zinc electrode connected with the positive pole is pressed upon the lint, and a current of not less than three milliamperes per square centimetre of surface under treatment is passed for from twenty to thirty minutes. When the treatment is complete the surface of the ulcer should become coated with a dead-white layer. Owing to the importance of using a sufficiently large current to drive the zinc ions effectively into the diseased tissue we prefer to carry out the operation under light anæsthesia, especially when the edges of the ulcer are much thickened, as in this case it is advisable to pierce them with a zinc needle in order to destroy the deeper parts.

Provided that the disease has not extended to the bone or cartilage, as we have already said, zinc ionisation is a very satisfactory method of treating rodent ulcer, and a cure can be relied upon in the majority of cases. The cosmetic results are also better than with any other method except carbon dioxide snow.

Sciatica. — Sciatica frequently proves very intractable to ordinary methods of treatment, and some form of electric treatment is often of service in such cases. We have seen good results from the use of the Schnee foot-baths, the anode being connected with the painful limb, and also from the application of the roller electrode. If preferred, ionisation with sodium salicylate (2 per cent., negative pole) may be tried, and is often successful; pads soaked in the solution are applied to the course of the sciatic nerve, and large currents are employed. Recently, however, we have been successful with X-ray treatment in these cases.

Superfluous Hairs.—The treatment of hypertrichosis by electrolysis is a tedious business, as each separate hair has to be attacked separately. The needle must be passed right into the hair follicle, and no attempt must be made to extract the hair until the follicle is completely destroyed; this requires fully a minute, although the hair is easily pulled out at the end of about thirty seconds. The operation is a little painful, but an anæsthetic is not required. Not more than a dozen hairs should be removed at one sitting.

This method of treatment is a successful one of getting rid of the disfigurement, but requires a good deal of patience and not a little fortitude on the part of the patient. There is always regrowth of some of the hairs, even when the greatest care is taken to destroy the follicles, and these will necessitate further treatment.

Ulcers.—Chronic (non-malignant) ulcers may be treated by ionisation of zinc or copper. In either case a 2 or 4 per cent. solution of the sulphate is used, and is applied through pads backed by an electrode of the same metal. The effect of the ionisation is to make the surface cleaner and to promote healing. In varicose ulcers it is often very successful.

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CLIMATOLOGY AND BALNEOTHERAPY

Climate as a means of treating disease has been utilised from the earliest times, and an enormous mass of literature has grown up upon the subject. From the present standpoint, however, the question has to be largely reconsidered. The virtual goal of all climatic treatment in the past was the cure or alleviation of phthisis. In recent years the introduction and universal adoption of the sanatorium method of treatment have practically relegated climate to a very minor position in the treatment of this disease. There will always remain a certain percentage of cases in which sanatorium treatment can be reinforced and often led to a successful issue by a change of climate. But at the most these cases will bear a small proportion to the total, and the clinical rules and cautions which fill the works of ten or twenty years ago need not detain us here. The aim of the present article is to describe, in brief, those regions which experience has shown to be of value and to indicate the diseases which are likely to benefit most from a stay in any given locality. Change of air may affect its object in two ways, on the one hand by removing the patient from conditions which produce and prolong his morbid state, as when a bronchitic

subject is removed from the fogs of London, on the other, when some definite physiological effect is sought, as when the jaded worker is sent to the bracing air of the Alps. Actually the effects are largely intertwined one with the other. For practical purposes climates for the invalid had best be considered as regards the districts which are most frequented than from purely geographical features. We may therefore consider—

The Climate of the Swiss Alps.
The Climate of Egypt.
The Climate of the Mediterranean Coast.
Home Climates.

The Swiss Alps.—The main features of such climates are low barometric pressure, and great diathermancy of the sun's rays. In winter, when once the snow has fallen, the air is singularly still, cloud is rare, and fog entirely absent. Owing to the sparse population and the presence of snow through a greater part of the year, the air is singularly free from impurities. The cold is in winter considerable; in Davos, for instance, the mean temperature is 18·6 in January and 29·3 in November, while the relative humidity varies from 79 to 84 per cent. In the still clear air of the Alps this considerable degree of cold is only felt as a pleasurable tonic. The physiological effects of the climate are in the first place those of altitude, as evidenced by breathlessness and rapid pulse, notably increased on exertion, headache, and often insomnia. Given that the individual has adequate powers of accommodation, the pulse within a few days becomes slower and firmer, the respirations deeper. Further, both the hæmoglobin and the corpuscles tend to increase, and the amount of water and CO_2 exhaled from the lungs is increased, notably so during the winter months. Other than these mechanical effects of diminished pressure the dry cold air produces a very marked influence on appetite and digestion, which are both improved, with a concomitant increase of nervous energy. These symptoms indicate a marked stimulus to metabolism, both through circulatory changes and by way of direct nervous stimulation. The therapeutic benefit to be gained depends on the patient's power of response to stimulus. With sound heart muscle, elastic arteries, and no marked toxæmia, nothing but good can result from a sojourn in the Alps in a very wide variety of ailments. The power of bearing cold can best be judged from the circulation: persons with cold hands and feet, with high blood pressure, or above all, with a ventricle beginning to fail behind old-standing high tension, rarely get benefit. The local physicians have long noted that patients with very rigid chest walls rarely can bear the cold of an Alpine winter. But given that the patient has the necessary natural caloric and sufficiently elastic arteries to emerge successfully from the trial of accommodation, the good to be obtained is very great. The clinical features of the cases of phthisis which are most suitable we shall refer to later. But for cases of bronchitis occurring in middle life, when degenerative changes are only just beginning, a sojourn may entirely obviate drifting into a chronic condition. Conditions of neurasthenia due to overwork derive the greatest benefit. In enumerating the individual resorts, it would seem advisable only to mention those to which invalids in the main resort, rather than the numerous centres devoted entirely to winter sports. Davos, 5200 ft., less windy, but not so sunny as some others, is probably the best equipped of all the resorts for the treatment of serious cases. St. Moritz, 6000 ft., is more sunny, but with greater exposure to wind. The other resorts in the Engadine, Pontresina, Samaden, Sils Maria, Maloya, present certain slight differences one from the other, but the main climatic conditions are the same. Arosa, 6100 ft., a very sheltered spot, with a large proportion of sunlight, is admirably equipped for the treatment of phthisis. In French Switzerland, Leysin, 4712 ft., above Aigle, sheltered from the wind with a sunny outlook, has great merits. Caux, 3580 ft., above Montreux, Les Avants, 3290 ft., and Château d'Œx, 3650 ft. all being better adapted for patients who are unable to bear the more exacting physical demands of the higher levels.

A series of lower resorts, such as Evian, Montreux, Glion, Territet, may be mentioned. Situated on the shore of Lake Leman, they are fairly sunny and free from fog, and form ideal spring and autumn halting-places, and have the further advantage that they are within easy reach of mountain stations of almost every altitude. Meran, with Obermais, in Tyrol, at an elevation of 1000 ft., is also a sunny and bracing spring and autumn resort.

Allied to the climate of the Swiss Alps are the resorts of the Rocky Mountains, but they have comparatively few sanatoria, and the chance of an invalid earning a living there is infinitely more precarious than at home.

Egypt.—The climate of Egypt, although it is only available for a few months in winter, is one of the most delightful in the world. Warm days, with constant sunshine, no mist nor fog, and practically no rain, and a very dry atmosphere, constitute an almost ideal climate for those of low vitality. The only drawbacks are the contrast of sun and shade, and winds—the cold northerly wind and the Khansin, a very enervating southerly wind—and the discomforts of an occasional dust-storm. Cairo is too large a

town for invalids other than jaded or neurasthenic patients; for them the changing scenes of an entirely new world provide a wholesome stimulus. Mena House, near the Pyramids, has a charming climate up to April. Helouan, situated in the desert sixteen miles from Cairo, with sulphur springs and good bathing accommodation, affords all the advantages of desert air, coupled with the unique possibility of a bath cure during the winter months. Luxor, 450 miles south of Cairo, is warmer and drier than Lower Egypt. Assouan, again, at the first cataract, is still warmer than Luxor, and, further on, Khartoum is warmer still. Upper Egypt though warmer is available for a shorter time. Practically the bulk of invalids follow the season from Lower to Upper Egypt and back again as the sun gains in power. Another charming method of enjoying the climate is the Nile steamer or the more costly and luxurious dahabeah.

Rheumatoid arthritis, bronchitis, renal and heart diseases, probably find the best environment in the world in Egypt. The calls on all the functions of the body are reduced to a low ebb, and the feeble powers of the old or weakly are conserved.

The Mediterranean Coast.—The seaboard of the Mediterranean presents a variety of climates —of these the Riviera, both from its remarkable natural features and great popularity, may be considered first. A gigantic undercliff was Henry Bennett's description of this region, and an apter phrase was never coined. A narrow strip of land, from one to five miles in width, bordered on the one side by the sea and on the other by mountains which rise steeply to a height of 1500–2000 ft. and pass backwards tier after tier to the main chain of the Alps. With minor variations this configuration stretches from Toulon to Spezzia, and it is to this mountain barrier that the peculiar features of the climate are due. Each town lying under the lee of the mountains, the shore bathed by a warm sea, while the bright sun not only warms it by day but insures the warmth being kept up at night by radiation. Such conditions confer warmth greater than less-sheltered regions in the same latitude. Fog is absent, and the rainfall, though almost equal to that of London, is concentrated into about a third of the number of rainy days, while the relative humidity varies from 65 to 75 per cent. as against 75 to 85 per cent. in London. But with these merits there are corresponding drawbacks, and the most notable of these are the cold winds which sweep through the passes of the mountains and become diverted in a direction parallel to the coast. A further danger to the invalid is the very marked difference between sun and shade temperature, and the very rapid cooling at sunset: a drop of nine degrees in five minutes may be experienced. The physiological effects are tonic, and to some extent exciting to the nervous system; digestion and appetite are generally improved, but sleep is apt to be interfered with. The virtues of the climate are, in the first place, that a very diminished call is made on the power of reaction, and in the second, that absence of fog and dryness of the air exercise a beneficial effect on any bronchial or pulmonary trouble. The best months are from mid-October to mid-May; after this the heat becomes too great for invalids to derive benefit. The individual resorts differ in the character of their climate, largely as they are nearer or farther from the sea, or as mountains are immediately behind them or at a greater distance inland. Hyères, near Toulon, the most westerly, is situated some miles from the sea and at some distance from the mountains. St. Raphael and Valescure, the former situated on the seashore, the latter some two miles inland amongst the pines, are bracing and well adapted to the vigorous. Cannes, the most fashionable of all the resorts, stretches over a wide area, the mountains being some distance inland. Consequently it is colder than some other resorts, but definitely more bracing. Grasse, further back in the hills, at an elevation of 1500 ft., forms an admirable place of change for those who tend to flag at the lower levels. Thorenc, 4000 ft., is of great value as an accessible summer resort. Nice, a large town with the charming suburb of Cimiez on a spur of the mountains, is essentially a pleasure rather than a health resort. Beaulieu and Monte Carlo are very sheltered and sunny; at Mentone, the cradle of the reputation of the Riviera, the East Bay is the most sheltered and warmest spot on the coast. Then, crossing the frontier into Italy, we come to Bordighera, more open and colder, and more bracing. Further on, San Remo, only slightly colder than the East Bay of Mentone. Alassio, bracing and more rural in its surroundings. Beyond Genoa the climate changes and is more humid and sedative. Pegli, Rapallo and Santa Margherita are all sheltered and sunny. Florence and Rome may be mentioned, but are in no sense climates for invalids other than the attractions afforded by a considerable degree of sunshine and wealth of artistic treasures. Naples, with Sorrento and a few stations along the adjacent coast, is warm though variable and rainy, and hardly adapted for invalids. Sicily is warm, somewhat wet and extremely variable, bright sunshine, cold winds and rainstorms often succeeding each other. The natural beauties and relics of the past make it an ideal resort for the elderly or the neurasthenic. The island of Corsica is warmer than the Riviera and some-

what more humid; the town of Ajaccio is sheltered, and forms an attractive and healthy winter station for bronchial cases.

Algiers is warmer than the Riviera, the mean winter temperature being 57·3, there is less contrast of sun and shade temperature, and the rainfall is greater, amounting to some forty inches. Bronchial and asthmatic cases do well there. Mustapha Superior, a suburb of Algiers, has good accommodation. A more bracing station is Hamam R'Irha, situated at an elevation of 2000 ft. in the lesser Atlas Mountains. At Biskra, again, a day's railway journey inland, the full benefit of desert air is obtained; it is therefore well adapted for rheumatic cases. Further westward, Tangiers, which is more under the influence of the Atlantic than that of the Mediterranean. Gibraltar, with the new resort of Algeciras over the Spanish lines, is sunny but windswept, and has the humid character of the Atlantic seaboard. Malaga, on the south-eastern coast of Spain, is warm and dry and well protected, but the accommodation is poor. The Balearic Islands have a very warm, dry and bracing climate, with fair accommodation. Madeira, in the Atlantic, has a remarkably equable temperature. The mean winter temperature being 61 and summer 69, it is admirably suited to persons of low vitality. The Canary Islands, Teneriffe and Grand Canary resemble Madeira in equality, but are drier and more bracing.

A few other localities in the south of France may be mentioned here. Biarritz, situated south of Bayonne, is sunny and experiences all the bracing influence of the Atlantic. Arcachon, south of Bordeaux and on the confines of the Landes, surrounded by pine woods, is warm, moist and remarkably sedative. Pau, between Bayonne and Toulouse, is warm, sunny and unusually windless; it is well suited for bronchial and many neurasthenic cases; the climate is notably sedative. Vernet les Bains, thirty miles from Perpignan, near the Spanish frontier, with its sulphur springs of various temperatures, has a dry and mild climate, which enables bath treatment to be carried on during the winter months.

The Health Resorts of the British Isles may be divided into the tonic or stimulating and the sedative, warm and sheltered. The bracing seaside resorts are situated for the most part on the East Coast, which is also the driest part of England. Margate, Broadstairs and Ramsgate are very bracing, and have acquired a well-deserved reputation for the beneficial effects of the climate on enlarged glands and surgical tuberculosis generally, as well as for debility of all kinds occurring in children. On the other side of the estuary of the Thames we come to Felixstowe, well protected and sunny; Aldeburgh, Lowestoft and Yarmouth. Cromer and Sheringham look due north and have a great reputation for the jaded and overworked who can stand strong air. Bridlington, Scarborough, Filey and Saltburn are somewhat damper than the Norfolk resorts. In Scotland Stonehaven and Nairn may be mentioned. Inland resorts of a bracing character which are adapted for those whom the sea affects injuriously, such as the gouty and those suffering from certain forms of skin disease and some cases of insomnia, are typified by Malvern and Ilkley in England, Braemar and Aviemore in Scotland. The more sedative and sheltered localities of the south are of great value as winter quarters for cases of bronchitis, heart disease, persons with impaired powers of locomotion and feeble vitality generally—Hastings and St. Leonards, Bexhill in Sussex; Bournemouth, warm and very sheltered, as is also Ventnor in the Isle of Wight. In the West country, Torquay, Sidmouth and Falmouth are warm and sheltered. Tunbridge Wells has great merits as a warm and sheltered inland resort, well adapted for the same class of case as Bournemouth, but which is injuriously affected by the sea. Taken as a whole, the British resorts lack the bright sunshine and dry air of many foreign places; but, on the other hand, they do not overstimulate the nervous system as is the case with many foreign places and they have the merit of being available all the year round. As Charles II said, one can pass more time out of doors in England than in any other country in the world.

Having described the principal regions which are sought in search of health, the diseases likely to be benefited may be considered individually. **Bronchitis** in its more usual form, when an increased tendency to catarrh and emphysema is a sign of tissue degeneration, is much benefited by a sojourn on the Riviera. The absence of fog and the possibility of open-air life not only allow the bronchial mucous membrane to recover to some extent its normal tone, but also check degeneration by diminishing the demands on metabolism. When the cough is dry, and expectoration scanty, Madeira, the Canary Islands, Algiers or Corsica are indicated. Winter cough beginning in early middle life is benefited far more by a sojourn in the Alps than anywhere else if the patient is sufficiently robust. Egypt, although available for a shorter period of the winter, is probably the best climate for the senile form.

Asthma is notoriously capricious, and has to be considered both from its nervous and bronchial aspect. Pure nervous asthma in a young adult is often strikingly benefited by a sojourn in the Alps or by treatment in the summer at Mont Dore (see later). For the more bronchial type, the Riviera at some

elevation from the sea or Egypt is more suitable.

The chief influence of climate in **diseases of the heart** lies in the avoidance of bronchitis or broncho-pneumonia, consequently Egypt, Algiers or the Riviera are indicated. High altitudes are in the main contra-indicated, though some cases of bradycardia in early middle life are strikingly benefited by a graduated ascent to a high altitude, and by carefully regulated exercise. Most cases of heart disease are injuriously affected by a sea voyage.

Rheumatoid arthritis derives more benefit from a winter spent in Egypt than any other form of climatic treatment. Failing this the Riviera or Algiers, where the open-air life improves general nutrition, and the rheumatic pains are generally benefited by the dry atmosphere. At home, the dry air of the East Coast gives the best results.

Gout is benefited by a warm climate, whereby the strain on the kidneys is relieved, while general metabolism is improved by the open-air life. Egypt, the Riviera or Algiers are the most favoured resorts. In our own climate gouty conditions are apt to be aggravated by the sea air.

Diseases of the kidneys derive marked benefit from residence in a warm climate. Cases of nephritis, whether parenchymatous or interstitial, often show the most surprising improvement. The increased action of the skin has a notable effect both on the amount of albumen and the general symptoms, such as headache and dyspepsia. Egypt, the Riviera, Algiers, and for patients who bear voyages well the Canary Islands or Madeira are the most suitable places. It is essential that the sojourn should be made as long as possible, and that the return to England should be made sufficiently late. No class of disease is more adversely affected by sudden change from warmth to cold.

Diseases of the Nervous System.— Organic diseases such as tabes or sclerosis only derive benefit in so far as an open life is possible for them in a warm climate, such as Egypt, Algiers or the Riviera.

Hemiplegia equally benefits in as far as a warm climate benefits the concomitant arterial degeneration.

The sufferers from that medley of functional morbid conditions which are for convenience grouped under the heading of **neurasthenia,** are for ever trying change of climate as a refuge from their miseries. When the circulation is good and the patient vigorous, he should be sent to the Alps, unless insomnia is a marked symptom: given that he sleeps and can and will take exercise, the constant stimulus of air and altitude will do more to restore him to health than any other form of treatment. In cases where the hands and feet are cold and the blood pressure low, Egypt or the Riviera, Rome, Florence or Sicily, may be tried, but here again it is essential that insomnia is not a marked symptom. Then the artistic treasures of Italian cities or the gorgeous colouring of the East may give them fresh ideas and break the habit of what the French describe as "listening to themselves live." Where insomnia is a marked symptom Pau or Arcachon may be tried, otherwise it is better to try one of the English resorts, the East Coast in the summer and one of the southern or western resorts in winter. Malvern and Ilkley and Braemar are also of great service in such cases. A word of caution must be given against sending these cases for sea voyages should they show that not uncommon symptom unreasoning terror, for the fear of drowning aggravates the situation: the writer has seen the most pathetic instances of demoralisation occurring in mid-ocean. Venice and the Italian lakes at certain seasons are of the greatest value in that form of neurasthenia engendered by definite hard work.

Neuralgia and Migraine are benefited by a dry and warm climate such as Egypt or the Riviera. They rarely benefit by high altitudes.

Diseases of Digestion are benefited by change of climate in so far as they depend on some secretory or motor failure of nervous origin. Flatulent dyspepsia often shows striking improvement at high altitudes. Dyspepsia due to slow digestion is also benefited by a sojourn in Rome or Florence, the Riviera. Mucous colitis is benefited by removal to a warm climate—preferably Egypt or the Riviera—where intestinal spasm, and dyspepsia are notably lessened.

The climatic treatment of **phthisis** at the present time presents considerable difficulties, as outside the admirable sanatoria at Davos, Arosa and Leysin the difficulty of finding accommodation is very considerable. Early cases with limited disease who make but slight progress in sanatoria at home may derive increased benefit from going to the Alps. It is not necessary here to indicate the class of case which will be suitable or unsuitable, since in the majority of instances the patient will have undergone a period of probation at a sanatorium. Cases which have become partially arrested or cannot bear the cold of open-air life in England and those with dilated bronchi and constant attacks of bronchitis derive the greatest benefit from a sojourn in Egypt or the Riviera. California affords a good climate for partially arrested and fibroid cases, but it must be borne in mind that the chance of earning a livelihood is even slighter than at home. Bronchiectatic phthisis derives great

benefit from the Alps, or, if complicated with much general bronchitis, from Egypt or the Riviera.

The advanced cases should never be sent away unless with full knowledge of the probable result, and with means for every comfort. Then Madeira, Egypt or the Riviera may be tried. But, as Sir Thomas Browne said, "he found the most healthful air of little effect where death had set her broad arrow."

The climatic treatment of **diseases of the throat** is in the main directed to cases of simple pharyngitis or laryngitis in which removal from adverse conditions such as damp or fog will of themselves effect a cure. Egypt or the Riviera, or, where there is much dry cough, Madeira, the Canaries or Corsica are preferable.

Finally, we have to consider how far those slow degenerative changes which we call growing old can be alleviated by change of climate. A man is as old as his arteries, and when the effects of high blood pressure and subsequent arteriosclerosis begin to make themselves felt, whether in wind or limb or instability of nervous system, the time has come to lessen the stimuli to increased work. The whole subject has been treated with consummate literary skill by Dr. King Chambers. The practical point is that when degenerative changes become manifest the patient should be removed to a warmer climate for the winter, Egypt, Algiers, or the Riviera. Probably the open-air life and diminished calls on his metabolism will enable him to lead a moderately active life for some years. With increasing feebleness a journey abroad will be less and less advisable, but in the mild atmosphere of Bournemouth, Torquay, or Falmouth, he may still maintain a fairly active life for many years beyond his allotted span. M. G. F.

HYDROLOGY

By the term Hydrology we mean the drinking of waters more or less impregnated with mineral substances at their fountain-head. A further development of this process is bathing in the waters, or their application as douches, sprays or enemata. And yet a third is the application of other substances such as mud, peat or fungi to the surface of the body. In the first place it must be conceded that the effect on metabolism which is observed from drinking waters is in no sense proportional or, indeed, comparable to the therapeutic action of the salts which they contain. The discovery of radium has to some extent cleared the ground and given scientific sanction to the old view that a natural mineral water was a thing *sui generis*, and to be used according to the traditions of experience rather than in conformity with the theories of pharmacy. Within the scope of this article a classification of waters according to their chemical characters would serve no useful purpose. Practically, we know that some are purgative and diuretic, others contain sulphur, iron, or arsenic, while others again, of great value, would appear to be natural hot water containing very little in the way of chemical constituents. On the other hand, the higher the proportion of chemical constituents, the more potent as a rule the effect of the water, each in its own way according to its chemical character. The most feasible plan of indicating the effects of mineral waters would appear to be to discuss them under the heads of individual diseases for which they have been found to be indicated. Baths may act in many ways, either by their natural action upon the skin as sulphur baths in eczema, or, from the gas which they contain by its mechanical effect in dilating the capillaries of the skin. To a large extent baths are used in the form of douches, which enable forcible massage to be used with less pain to the patient and consequent relief to stiffness and pain about inflamed joints or muscles. Immersion baths of peat or mud are of great value in soothing the pain and lessening the induration about old inflammations such as sciatica, lumbago and neuritis, or old pelvic and peritoneal adhesions. Different mineral waters may be pulverised and used as sprays for the throat, nose or ear, clearing away adherent mucus, and paving the way for the mucous membrane to resume a more healthful vascular condition. In like manner, by their carefully regulated use as enemata, the lower bowel may be cleared of mucus and intoxication of the whole system lessened. The vagina may also be markedly benefited by immersion in a bath with a speculum *in situ*. Many spas have grown to great repute for the treatment of particular maladies largely owing to the shrewdness and ingenuity of the local doctors in devising fresh methods of local hydrotherapeutic treatment. In discussing the individual classes of disease it is only possible to mention the main spas for which each is suitable.

Disorders of Digestion. — Spa treatment in these affections is to a large extent the treatment of abdominal plethora, the result of a succession of feasts coupled with too little exercise which the fashionable season of every capital in Europe is apt to engender. Homburg, with its mildly purgative waters and well-managed régime, Marienbad, Kissingen in Germany, Vichy in France enjoy a well-deserved reputation. In England Llandrindod, Harrogate or Leamington, and in Switzerland the charming mountain resort of Tarasp may be recommended. For the dyspepsia of anæmic

young women, Schwalbach or St. Moritz are indicated.

Diseases of the Liver.—Cholelithiasis, and portal plethora, notably that produced by residence in the tropics, derive great benefit from the natural hot sulphate of soda springs of Carlsbad. Vichy or Brides in Savoy; Leamington, Llandrindrod, Buxton or Harrogate in England; and Strathpeffer in Scotland give good results.

Diseases of the Intestines.—At Plombières was first instituted a definite plan of treatment for washing out the colon by carefully arranged machinery, aided by the use of under-water massage to the abdomen to lessen spasm. The success which attended this attempt to treat a disease previously considered hopeless has led to its adoption at many other spas, such as Luchon, Vichy, Harrogate, Buxton and Bath. The results obtained have certainly justified its adoption.

Diseases of Urinary Organs.—For gravel and different forms of nephrolithiasis, Contrexéville, and Vittel in the Vosges, have attained the greatest celebrity; Monte Catini in Tuscany also is of distinct value. For diseases of the bladder and prostate, Wildungen in Pyrmont has a great reputation; the waters are earthy and are drunk in large quantities, but not a little of its undoubted success is due to the skill of the surgeons who practise there.

Diseases of the Circulation.—In the first rank comes Nauheim, with its baths charged to a high degree with natural carbonic acid gas. The value of the treatment in cases of valvular disease and dilatation due to high tension is undoubted. Most spas or therapeutic institutions now have installed baths impregnated with artificial carbonic acid gas. These have decided value, notably in anginal or severe cases for which a long journey would be too risky. It must be admitted, however, that for earlier cases the natural waters are markedly superior in their action to the artificial ones. In France, Royat possesses naturally aerated waters, which are used in much the same way as at Nauheim.

Diseases of the Respiratory System.—The spa treatment of these diseases consists essentially in the administration of sprays or nasal douches of mineral waters, whereby the pharyngeal or bronchial mucous membrane is cleared from mucus and stimulated. At Ems the system is very carefully carried out, machine-driven sprays of varying strength and fineness are applied to the throat or nose, while supplementary pneumatic machines are used to increase the play of the lungs and rectify the evil effects of emphysema. The effects of this treatment, combined with the interdiction of all tobacco and the undoubted value of the waters, have a most marked effect on cases of bronchitis, asthma and pharyngitis. Cauterets, in the Pyrenees, has somewhat the same system with sulphur water, and at Mont Dore, in Auvergne, the sprays of alkaline waters are combined with the drinking of arsenical waters. The same system of inhalation has been installed at Bath, Buxton and Harrogate. At Salso Maggiore in Lombardy, inhalations of bromo-iodine water are given; the patients also sit for a considerable time in an atmosphere saturated with the spray of this water.

Diseases of Women.—The effects of past pelvic inflammation were first treated at Franzensbad by peat baths with marked success, a method which has been copied at many other spas. Considerable success has resulted from the Bromo-Iodine baths at Woodhall Spa, Kreutznach, and Salso Maggiore in cases of simple congestion.

Diseases of the Joints.—The spa treatment of gout resolves itself into either relieving plethora by purgative and diuretic waters, or the use of sulphur waters which are claimed to have a direct effect on metabolism. For the former purpose Homburg, Carlsbad, Tarasp, Kissingen and Vichy are all of value. In the second category, in which the arthritic symptoms predominate over the digestive ones, the Pyrenean springs have considerable merits, the principal spas, Luchon and Cauterets, having admirable installations. At home, Llandrindrod Wells, Harrogate and Strathpeffer, yield good results.

The variety of pathological conditions which for convenience may be grouped under the name rheumatoid arthritis, are benefited by spa treatment in a twofold manner, constitutional and local. In the first place the ingestion of waters lead to the elimination of waste products. In the second place various forms of local treatment have been evolved at different spas for the relief of pain and stiffness. Aix-les-Bains in Savoy early adopted the method of massage carried out under a stream of water, a system said to have been brought back from Egypt by Napoleon's troops. The same method has been adopted at most spas which were resorted to for arthritis. In addition to Aix, Vichy, Baden-Baden, Schinznach in Switzerland may be mentioned. Bath has radio-active waters and a good winter climate, so that treatment can be carried out during the winter months. Other British resorts are Buxton, Harrogate, and Strathpeffer in Scotland. Another method of treatment is immersion in peat baths, which yields admirable results, notably in cases of sciatica. These originated at Franzensbad, but are used at Marienbad, Carlsbad, Strathpeffer, Harrogate, Llandrindod Wells and Buxton. Immersion in brine baths forms a valuable form of treatment at Droitwich, Reichenhall and other

spas. At Acqui, in Piedmont, the application of hot mud soaked in sulphur water, either to a single joint or to the whole body, produces good results.

Diseases of the Nervous System depend in the main on the treatment of some underlying constitutional condition. Headache and neuralgia is often cured by a course of sulphur waters. At Lannalou in France great relief is afforded to the pains of tabes from effervescent baths. The different forms of neuritis are best treated by the same methods as those applied to rheumatoid arthritis.

Diabetes and Glycosuria derive benefit from the waters of Neuenahr, and when due to gouty conditions from sulphur waters.

Diseases of the Skin are benefited on the one hand from the internal use of waters to lessen a gouty tendency, and on the other by prolonged immersion in baths of mineral water. Sulphur baths are the most generally useful, and those of Schinznach, Strathpeffer and Harrogate enjoy a well-deserved reputation. M. G. F.

TREATMENT OF ELEMENTARY SCHOOL CHILDREN

The Medical Inspection of Elementary School Children, although a natural corollary of Elementary Education, is only of recent and gradual growth. It was first necessitated by the provisions of the Special Schools Acts of 1893 and 1899, although two cities had previously appointed School Medical Officers, but it was only after the passage of the Elementary Education (Administrative Provisions) Act of 1907 that it became a compulsory duty of all Education Authorities to appoint School Medical Officers, and to carry out routine inspection of the school children. By the provisions of this Act, which came into force on the first of January, 1908, every child must be examined immediately before or as soon as possible after admission to school, and at such other times as the Board of Education may require. The present policy of the Board is to require also the examination of children shortly before they leave school and at an intermediate period, that is about the age of from eight to ten years. This Act also gives to the Local Education Authority "the power to make such arrangements as may be sanctioned by the Board of Education for attending to the health and physical condition of children educated in the public Elementary Schools," provided that they may encourage and assist the establishment or continuance of voluntary agencies to this end. This Act is therefore a very important one, for it is by its sanction that all medical treatment of school children is carried out by the Education Authorities.

Several other Acts of Parliament give powers which are important from the medical point of view. The Elementary Education (Blind and Deaf) Act of 1893 makes it compulsory upon all Education Authorities to provide accommodation for blind and deaf children between the ages of seven and sixteen in special schools. It also makes attendance at school on the part of these children compulsory. It is not sufficiently widely known amongst medical men that every deaf or blind child of poor family has a right to be educated. The Elementary Education (Defective and Epileptic) Act of 1899 permits a Local Education Authority to provide special accommodation in school for mentally and physically defective children and for epileptics. Such provision is not compulsory, but where it is provided the parents of a child who is alleged to be defective have the right to demand that he shall be medically examined with a view to admission to the special school, and children who are certified to be defective can be compelled to attend the school between the ages of seven and sixteen. Every child attending such a special school must be medically examined at least once a year.

One other Act requires mention. The Education (Provision of Meals) Act of 1906 gives the Education Authority the power to take steps to provide meals for children attending the Elementary Schools and to co-operate with any Committee that undertakes such provision. It also empowers them to spend money on providing meals up to the extent of a halfpenny rate, and requires that the cost of the meals so provided shall be recovered from the parent, unless the Authority are satisfied that the parent by reason of circumstances other than his own default is unable to pay the amount.

In addition to these Acts which deal directly with Educational matters, the Local Education Authority can utilise the general clauses of the Children's Act of 1908 and other similar Acts in dealing with neglected and verminous children.

The treatment of Elementary School children, then, includes general medical treatment provided for children in the Elementary Schools, the educational treatment of defective children, the feeding of children in school and the treatment of neglected and verminous children.

General Medical Treatment

Medical inspection in the Elementary Schools has brought out clearly the fact that there are several important groups of diseases and defects which are extremely common amongst school children, which have an important bearing upon the education and prospects of the child, and for which there is at present a very

inadequate organisation for treatment. These defects include defective vision, diseases of the throat, nose and ear, specially enlarged tonsils, adenoids and otorrhœa, ringworm and the commoner infectious skin complaints, *e. g.* impetigo and scabies, and dental decay. In addition, the slighter (postural) curvatures of the spine, and general anæmia and debility, whilst they need not prevent attendance at an Elementary School, have an important bearing upon regular school attendance and educational treatment.

It will be evident that treatment for these defects, requiring, as it may, expert examination, operation, and special methods such as the use of X-rays for ringworm, could only be obtained by the poor through the hospitals; and the amount of routine work thus thrown upon the hospitals as the result of school inspection very soon became burdensome. The Board of Education has, therefore, sanctioned various special methods whereby this treatment may be secured at the expense of the Local Education Authority. The two methods which have been chiefly utilised are the institution of special out-patient departments at the hospitals, and the establishment of School Clinics.

Special out-patient departments for the treatment of visual defects, diseases of the nose, throat and ear, and of skin diseases such as ringworm, have now been established by many hospitals. The arrangements made are that the clinic is held at a special time (not at the ordinary out-patient time), that a certain definite number of children are sent for examination or treatment on each day so set apart, the School Care Committee being responsible for this, and that a salary is paid by the Education Authority to the medical man doing the work, and a capitation grant to the hospital for each child so treated.

School Clinics, properly so-called, are established and paid for by the Local Education Authority, the medical officers of the clinic being appointed by that body and paid a salary. In some districts, however, the local members of the profession have preferred to attempt to keep this treatment at clinics under their own management. The clinic is then carried on by a local committee of medical men, who select and nominate the medical officers. The latter are paid a salary by the Local Education Authority, who also pay a capitation fee for each child treated to go towards the current expenses of the clinic. This latter system, while it is favoured by practitioners in many parts of the country, has been criticised by the Board of Education because it places the Treatment Clinics outside the direct control of the School Medical Officer for the district, and because by means of it school inspection and treatment are not very perfectly co-ordinated. It is at present recognised by the Board, but in the event of the latter withdrawing that recognition the Treatment Centres so established would have to be closed.

Diseases of the Eye.—Children are referred to the clinics from the schools on account of defective vision, squint, simple external diseases of the eye, and diseases of the lids. The standard of defective vision requiring treatment is usually taken as six-eighteenths or worse with either eye for children in the lower classes, and six-twelfths or worse with either eye for children in the upper classes. It is most important that the treatment thus arranged for children suffering from defective vision should not stop at the prescription of glasses. It is customary for an arrangement to be made whereby a spectacle maker attends at the clinic, and the Board of Education have sanctioned arrangements for the provision of spectacles by the Local Education Authority, provided that every possible endeavour has been made to obtain them by the parents, or through voluntary associations. Further, it is most important that the school teachers should see that the children wear the glasses provided, and arrangements should be made for the re-examination of the children at intervals. Except by the correction of defective vision in one or both eyes, little or no attempt has up to the present been made to treat squint in School Clinics. The other eye diseases treated are blepharitis and the simple forms of conjunctivitis. The more serious diseases of the eye have to be referred from the clinic to the hospitals.

Diseases of the Throat and Nose.—The large proportion of children treated under this heading suffer from nasal obstruction, most often as the result of adenoids. This condition is so frequent that the treatment of it constitutes a serious burden upon the hospital out-patient departments, and at the same time it is serious in its results both from the physical and from the educational point of view. The treatment of adenoids has therefore become a recognised function of the School Clinic. The removal of enlarged tonsils may be grouped with it. These operative procedures of course necessitate a theatre, a waiting-room and a recovery-room. A surgeon, anæsthetist and two nurses can comfortably manage about ten operations in an afternoon in a clinic; in a hospital, with ample accommodation and more nurses, fifteen to twenty can be performed. It is most important where adenoid operations are being performed that one or two beds should be available, so that children can be kept under observation for a night if necessary.

The treatment of adenoids is not completed

with the operation. It is most necessary that proper methods of breathing should afterwards be taught. The children must be collected together either at school or at the clinic for daily breathing drill. This should begin with the clearance of the nose by proper use of the handkerchief; breathing exercises, both simple and combined with arm and trunk movements, being then carried out for ten to fifteen minutes. In some cases, when the chest is flat or deformed, passive chest expansion movements combined with deep breathing exercises are also desirable.

Diseases of the Ear.—Under this heading practically only cases of chronic suppurative otitis media come under treatment. These are very frequent among school children, and the ordinary hospital out-patient treatment, consisting of the prescription of a lotion to be used at home for syringing or for instillation, has been proved to be very inefficient. Yet it is known that a large proportion of such cases can be completely cured by methods of ordinary cleanliness. The defect is not in the method of treatment but in the thoroughness with which it is carried out at home. If the clinic is to treat these cases satisfactorily, the syringing, etc., must be carried out by a nurse, either at the clinic itself or by the nurses visiting the children in their homes. Both these methods have been tried and have proved highly satisfactory. Cases which do not respond to such treatment, thoroughly carried out for three months, had better be referred to a hospital, as more drastic steps will probably be required.

Diseases of the Skin.—The most important of these is ringworm, which, owing to the difficulty of securing a complete cure has in the past been responsible for frequent prolonged absences from school. It has now been amply demonstrated that X-ray treatment is the most efficacious and in the end the most economical method. In Bradford it has been found that by this means the period of treatment is reduced on an average to 30 days, and the absence from school to 35 days. Treatment by the older methods resulted in an average loss of school attendance of 287 days. X-ray treatment properly carried out is absolutely safe, the scalp is free from infection as soon as the hair has fallen out, and the hair should be well grown again at the end of three months.

The other skin diseases treated consist of scabies, impetigo and similar infectious complaints. Their treatment requires no special comment.

Spinal Curvatures.—Those who have systematically examined a large series of school children for spinal curvatures have found that from 16 to 25 per cent. of the children could be classed as showing some degree of curvature. Only a very small proportion of these showed a structural curve, the large majority showed only a postural deformity, capable of correction when the child was shown how to stand or sit correctly. It is these common postural curves which require treatment in school or in the clinic; the structural curves are unsuitable for such treatment. Two methods are in use for organising this treatment. The first is by means of a special exercise class held daily for not more than ten children at a time in the school. The second is by similar but perhaps more individual exercise treatment at the clinic. In the first case the exercises must be carried out by one of the school teachers, who must first be specially instructed. In the second case it will probably be possible to secure the services of a trained instructress. The simple method of ascertaining in each case what type of treatment is required is to determine whether the posture assumed by the spine is one which the normal spine can assume. If it is not, then the curve is a structural one, and it will be more satisfactory to recommend hospital treatment. If the curve is one which can be imitated in the normal spine, it must then be determined whether the child by careful instruction can be induced to hold himself in a correct attitude. If he can, then class exercises carried out daily in school will be effectual; if, however, he cannot manage to get into a good attitude it will be better for a time at least to give him individual exercises in the clinic.

Dental Disease.—Medical inspection has amply demonstrated the great prevalence and importance of dental decay amongst children. The ways of combating this are briefly three: first, by altering by educational means the diet in infancy and early childhood and rendering this more suitable; secondly, by encouraging the use of the toothbrush amongst Elementary School children, and thirdly, by arresting dental decay at its commencement. The last necessitates the establishment of Dental Clinics, for there are, as a rule, no hospitals to deal with the work, and the payment of proper fees to a dentist is quite beyond the means of the parents of the average child. These clinics are still in the experimental stage, and to establish a complete system of treatment on these lines will necessitate a large organisation and will be a heavy expense. The experience so far obtained indicates that the treatment should be begun early, if possible before the age of six, that it should be preventive, temporary teeth being extracted whenever necessary, but permanent teeth preserved and filled, and that every child that has once been treated should be re-examined at regular intervals so that further trouble may be detected and treated in its early stages.

A Dental Clinic requires, of course, the

ordinary dental equipment for extractions and fillings. A dentist working five days a week may be expected to deal with a school population of 3000 to 4000 children.

Educational Treatment of Special Classes of Children

The classes of the blind and deaf children require only very brief mention. The definition of suitability for a special school is that the child is so blind as to be incapable of instruction through the ordinary visual channels, or so deaf as to be incapable of instruction through the ordinary auditory channels. There remain, however, a considerable class of children whose vision or hearing is so defective as to render them incapable of keeping pace with normal children, although they cannot be classed as completely blind or deaf. In the case of the partially blind also there is undoubtedly a risk that the strain of an ordinary school may further injure the eyesight and lead to complete blindness. Education authorities in certain large towns, recognising the impossibility of educating such children in the ordinary schools, have established special classes for the partially blind and partially deaf children.

Mentally Defective Children. — Mental defect in the educational sense indicates that whilst there is so low a mental status that the child cannot be educated with normal children, yet he is capable of attaining a certain degree of education, sufficient to give him a reasonable chance of becoming self-supporting; that is to say, he is not an imbecile or an idiot. The diagnosis of mental defect is often very difficult, particularly so in children who have been out of school and have never been taught. In addition to the consideration of the family history, medical and educational history and physical condition of the child, a careful mental examination is required. This should include investigation of the organs of sense, power of observation, memory, concentration and judgment, temperament, power of control and moral characteristics. Further, the educational attainments must be tested and considered in comparison with the normal, bearing in mind his age and his opportunities to learn. Various schemes of examination have been suggested. Of these the best known are the Binet tests. If a child is unable to respond to these tests as drawn up for an age two years less than his own, he is presumably mentally defective. One word of caution is necessary; these tests are drawn up on the supposition that they will be new to the child. As they get to be known they are used by the school teachers in testing the children in the Elementary Schools, the children learn them, and their value as a test of mental defect diminishes.

There can be no hard-and-fast line of mental defect. There must always be a proportion of dull backward children, and of children who are backward probably as the result of lack of educational facilities. For these there is an urgent need of intermediate schools or intermediate classes, into which the children can be drafted from the Elementary Schools, and in which their progress under more individual instruction can be noted. These classes give such backward children their chance of regaining their place in school, and render the diagnosis of doubtful cases of mental defect much more easy.

Physically Defective Children. — The term "physically defective" includes children who are crippled by tuberculous disease of the bones and joints, by paralysis and in other ways; chronic invalids, specially those suffering from heart disease and chorea, and anæmic debilitated children. Children who suffer from pulmonary tuberculosis may also be included as a special group.

A number of different classes of schools have been provided.

1. Resident Hospital Schools.
2. Resident Sanatorium Schools.
3. Country Recovery Schools.
4. Non-resident Day Schools.
5. Open-air Schools.
6. Trade Schools, Resident or Non-resident.

All these except the day schools necessarily include treatment for the physical condition of the children. Open-air schools require special mention. They are specially suitable for anæmic debilitated children, those suffering from slight heart lesions, and convalescent (non-infectious) cases of pulmonary tuberculosis.

The holding of the classes in the open air is only one part of the special treatment given in these schools. In addition the hours are long, from nine in the morning until six or later in the evening. Three meals, breakfast, dinner and tea, are arranged in school, a two-hours sleep is taken in the afternoon, and every child is bathed in school once or twice a week. The effect of these schools is therefore to put the children under good hygienic conditions for nine hours out of each twenty-four.

Treatment of Dirty and Verminous Children.— Two chief methods are utilised for endeavouring to improve the cleanliness of children. The first is to serve notices upon the parents stating in what respects the children are dirty, and directing how they may be cleansed. After two such notices, if no efforts to secure greater cleanliness have been made, the child is excluded and the parents prosecuted for not sending him to school in a fit condition. In the second method after the first notice warning the parents, the

child may be taken by a person authorised by the Local Education Authority, usually a school nurse, to a cleansing station and the child and his clothing cleansed. It is as well that the Sanitary Authority should at the same time cleanse the home.

School baths may be provided by the Education Authorities. On the Continent they are numerous; in England they are at present few, but are increasing. R. C. E.

TREATMENT BY MASSAGE, MOVEMENTS AND PHYSICAL EXERCISES

Massage consists in the treatment of some part of the body by friction, pressure or kneading. In ordinary massage these manipulations are carried out by the hand in various ways, but similar effects can be obtained by means of certain mechanical contrivances such as some forms of Zander apparatus, or by an electrically driven machine.

Methods of Manual Massage.—The ordinary methods of manual massage are—

1. *Effleurage*, i. e. stroking with the palm of one or both hands, or with the thumb and tips of the fingers. The stroking is always carried out from the periphery towards the centre, in the direction of the flow of venous blood; its effect is to increase this venous flow and also to increase absorption through the lymphatics, so that it assists in getting rid of inflammatory or traumatic effusions. Stroking has also a slight local analgesic effect.

2. *Frictions*, i. e. firm rubbing movements carried out in circles with the thumb or with the tips of the fingers. The effect is again chiefly to improve the local circulation, but friction has a deeper action than stroking, and to some extent indurated tissues and adhesions can be softened and stretched by deep friction.

3. *Kneading*, i. e. a muscle is lifted and kneaded between the finger and thumb or between the fingers and the palm, or between the two thumbs, or the whole limb may be squeezed and rolled between the two hands. The effect of kneading is evidently deeper than that of friction, and the mechanical effect is greater.

4. *Tapotement*, or percussion. The part is repeatedly and rapidly struck with the hands of the manipulator used alternately. The whole of the palmar surface of the hand may be used (clapping), or the tips of the fingers (punctation), or the ulnar border of the hand (hacking), or the clenched fist (beating). The effect is to produce a local hyperæmia which may extend deeply.

5. *Vibrations* are carried out by oscillatory pressure with the tips of the fingers over the line of a nerve trunk, or by similar movements of the whole hand, the palm being applied to the surface of the body; vibrations with the palm are chiefly used over the abdominal organs. The whole of a limb, *e. g.* the arm, may also be shaken by grasping the hand, fully extending the arm and shaking rapidly.

Vibratory movements can be readily and efficiently applied by means of an electrically or hand-driven vibrating machine. Such a machine should be capable of vibrating at the rate of 2000 or more vibrations per minute, and should be capable of adjustment so that the range and frequency of the vibrations can be altered. Many of the local circulatory and mechanical effects of massage can be obtained with such a machine.

These methods of massage produce their effects, then, chiefly upon the skin, subcutaneous tissues, muscles and other soft parts and upon the nerves. To a less extent the abdominal organs can be reached. In general the effects are to improve the local circulation, both mechanically by assisting the venous and lymphatic flow, and also by producing a local hyperæmia. The depth to which this circulatory effect is produced depends upon the method used. There is also a mechanical effect in deeper movements by which indurated tissues may be softened and adhesions stretched. Certain movements have, moreover, a local analgesic or soothing effect, whilst others, such as deep frictions, beating and vibrations if applied over nerves have a stimulating effect upon them.

Movement in treatment means the carrying out of normal movements of the joints within their normal range. They are of two main varieties, Passive and Active.

Passive Movements are carried out by the manipulator without any assistance from the muscles of the patient. They may be gentle, *i. e.* carried out within the limits of the movement permitted without resistance, or forcible, *i. e.* aiming at increasing the range of movement where this is not complete.

Active Movements may be simple (free movements) or they may be resisted by machinery or by pressure applied by the manipulator.

Resisted movements may be described as concentric or eccentric. Concentric are those in which the muscle or muscles concerned shorten, acting against an external resistance, *e. g.* flexion of the elbow by the biceps and brachialis anterior in opposition to a resisting force. Eccentric movements are those in which the muscles are stretched by an external force which they resist, *e. g.*, extension of the elbow by an external force, the biceps and brachialis anterior resisting and being gradually stretched. Eccentric movements may be very useful in the treatment of paralysed muscles which have not sufficient residual power to perform their normal work. For example, if

the biceps has not sufficient power to flex the elbow, it may still be exercised by making it resist whilst the forearm is supported and gradually extended.

Active movements may be supplemented by a passive stretching movement carried out by the manipulator at the end. Thus active flexion of the elbow may be carried out to the limit of possibility, and the elbow then forcibly flexed a little further.

All varieties of movements—active, passive, resisted or combined—can be carried out by the aid of machinery of the Zander or Pendel type, but practically everything that can be done by machinery can be done by hand and done with greater accuracy and delicacy. The chief use of such machinery is to reduce the labour of manipulation.

Movements may be carried out with several different objects. (1) To preserve the function of the joint. (2) To improve the function of a damaged joint by restoring its full range of movement. (3) To preserve or improve the strength or activity of a muscle or muscles. (4) For their effect upon the general health, *e. g.* to reduce obesity, to improve the circulation or for their mental effect.

Evidently the variety of movement used and the method of applying it must depend on the object to be attained. Whereas active joint movements will suffice to maintain the function of a joint, passive movements are necessary to increase it. Active movements may have several different effects upon the muscles according to the method of application. They may simply increase the strength of the muscles, or they may improve the rate of contraction, making the movements more rapid, or they may improve the control of the muscles, making the movements more accurate. It will be noticed that active movements have thus an important effect upon the nervous mechanism of the movement, and their use in this direction is often more important than their use to strengthen the muscles.

In order that active movements may be made to subserve their different purposes, certain points on their application require careful attention. In the first place, if the control of muscular movement is to improve it is important that the initial position from which the movement is to be carried out shall be correctly assumed, at first as the result of careful directions, later spontaneously. Further, the movement must be carried out accurately and in proper time. If muscles are to be strengthened to a greater or less extent, the work they are made to do in the course of a movement must be regulated, resistance, manual or mechanical, may be applied, or some method of altering the length of the lever moved by the muscle by shifting the centre of gravity of the part moved may be utilised. For example, a good exercise for the iliopsoas, rectus abdominis and other abdominal muscles is performed by lying on the back with the feet fixed and slowly raising the trunk to the upright position. The strength of this may be varied by altering the position of the arms. It is easiest with the arms by the side, more difficult with the arms at a right angle and the hands behind the neck (neck-rest position) and most difficult with the arms stretched upward above the head.

The difficulty of an exercise may be varied in another and quite different way. The initial position from which the movement is carried out may be altered, with considerable consequent variation in the difficulty of the exercise. There are five primary positions: standing, lying, sitting, kneeling, and hanging, as well as a number of positions derived from these. A given exercise may be very much easier in the sitting than in the standing position, because the support given to the pelvis in sitting relieves the patient of the necessity of maintaining his balance. Similarly, a trunk movement is easier in the stride position in which the feet are separated than in the ordinary standing position in which the heels are together and the feet turned out, and the exercise is made more difficult still by assuming the close standing position in which the heels and toes are in contact. In this example the exercise is made progressively more difficult by decreasing the base of support. Exercises in a position in which the base is small are called balance exercises, and are specially useful in improving the nervous control of the muscles involved.

By combining movements they may be made much more difficult. For example, a trunk and an arm movement may be carried out simultaneously, or a trunk movement may be carried out until a new position, requiring a certain muscular and nervous control to maintain it, is attained, and arm movements may be carried out in this position. The extra difficulty in these cases falls chiefly on the nervous mechanism of control, so that combined and complicated movements are of use chiefly in progressive training in co-ordination.

These principles, here very briefly stated, form the basis of methods of treatment by movements and by exercises.

Movements or exercises applied to a particular part of the body are used to obtain some particular local effect, *e. g.* to strengthen particular muscles or increase the mobility of joints. Their object will regulate their nature and mode of application. They are usually combined with massage, which should always be applied at the end of the treatment, and in the case of stiff joints at the beginning also.

In using more general exercises the effects of the treatment on the respiration, circulation and general health must be borne in mind. The table of exercises should as a rule begin and finish with breathing exercises, easier movements should be followed by more difficult, resisted movements involving considerable strain should be followed by free movements involving more rapid action. At the end of the table, massage should be carried out over the muscles which have been principally exercised, and the patient should then take half an hour's rest. The termination of all tables of exercises by breathing exercises and by massage greatly lessens the after fatigue, the breathing exercises improving the general, the massage the local, circulation.

General massage and abdominal massage require special mention. In general massage the patient lies on his back completely undressed but well covered with bed-clothes. Massage is then begun upon one lower limb working from the foot up to the groin, each joint as it is reached being put through active and passive movements. The other lower limb is treated next, then each arm in turn, working from the hand upwards. The neck and pectoral regions are next massaged, then the abdomen, and finally the back and buttocks. General massage should occupy from half an hour to an hour, the duration and the severity of the treatment being regulated in accordance with the condition of the patient. Each part as it is massaged must be carefully covered. General massage is used for many different purposes. Its effect may be soothing or stimulating, according to the methods employed. Frequently its use is as a substitute for ordinary forms of exercise which the patient is unable to take. The operator should always be conversant with the disease from which the patient is suffering and with the object of the massage.

Abdominal massage may also have several different objects. It may be used chiefly for its effects upon the abdominal muscles, or for its effect upon the intestinal tone and movements. These two constitute its most important objects, but it is also advocated for its effect upon the portal circulation, and for its effect upon the liver, kidneys, spleen and uterus.

The most useful abdominal movements are: deep circular kneading over the central part of the abdomen (the region occupied by the small intestine), deep kneading along the line of the large intestine from the right iliac fossa upwards to the right flexure of the colon, across the line of the transverse colon and down the left side into the pelvis. These two have a direct stimulating effect upon the intestinal walls and also a mechanical effect upon any collections of fæces. Frictions and stroking over the abdominal wall have also a stimulating effect upon the intestine as well as upon the abdominal muscles. Further, exercises for the abdominal muscles are useful in such a condition as chronic constipation.

Abdominal massage and exercises are also useful after abdominal operations, in patients who are confined to their beds, and in the treatment of obesity.

Treatment of the stomach, liver, spleen and kidneys are prescribed by some. It cannot be said that these have much to commend them, and if carried out roughly and unskilfully they might be dangerous.

Massage of the uterus, through the abdominal wall, to assist involution, is practised regularly by certain obstetricians. It is begun the day after the confinement and continued until the patient leaves her bed. Exercises for the abdominal muscles are useful in the later stages of the puerperium.

Massage and Exercises in Special Diseases

General Diseases.—General massage is of great use in the treatment of deficient nutrition in delicate people, specially those of sedentary habits, in anæmia of all sorts, in nervous diseases, in hysteria, during convalescence from acute or chronic disease, or after operations and in obesity. The massage must be graduated according to the condition of the patient and the stage of treatment. In obesity vigorous massage, especially vigorous kneading, is advisable.

Nervous Diseases.—In addition to massage which has an obvious use in maintaining the nutrition of the muscles, exercises are of special service in nervous diseases.

In hysteria exercises improving co-ordination and balance, and involving a certain amount of concentration, have great mental effect, and also assist in the treatment of local manifestations. Many hysterical deformities can be completely cured by carefully designed exercises. General massage is an essential part of the Weir Mitchell treatment.

In diseases of the lower motor neurone, such as poliomyelitis, massage of the affected muscles should be carried out from the first. Passive movements are necessary to prevent contractures and active movements to assist the recovery of paralysed muscles by functional use. Eccentric movement may be specially useful when the muscles are left too weak to carry out their normal concentric action. The same applies to neuritis and to injuries of the nerves. In neuritis and in nerves involved in cicatricial tissue vibrations (manual or, better, instrumental) over the nerve trunk are much used. Fine vibrations gently administered have a definite soothing effect and diminish the pain in neuritis. Stronger vibrations are said to

stimulate the nerve trunk; they almost certainly produce a hyperæmia in the nerve and assist in diminishing the fibrosis of a nerve in old-standing neuritis or in scarring after an injury. Massage and vibratory massage thus help to relieve the pain in old-standing neuritis or in painful scars and to improve the conductivity of the affected nerve. In progressive diseases of the muscles or lower motor neurones, such as progressive muscular atrophy and the various myopathies, massage has, of course, only a palliative effect. It will not stay the disease, but by maintaining the nutrition and functional use of the muscles it will diminish the rate of apparent advance.

In paralysis due to a lesion of the upper motor neurone massage and movement have to be applied upon a rather different principle. The diseases included in this group are for the most part of a fixed type and not progressive; as examples, infantile spastic paraplegia, diplegia and hemiplegia, and hemiplegia resulting from cerebral embolism, hæmorrhage or thrombosis, may be taken. The effect of these lesions upon the neuro-muscular system may be divided into loss of muscular power, loss of control (inco-ordination), spasticity, athetosis, stiffness of joints and trophic changes. The last two are more marked in the late-acquired than in the infantile cases. Stiffness of the joints and coldness of the extremity affected are attacked by the ordinary methods of massage, including the use of vibrations. Loss of power is similarly treated. But spasm and athetosis are not likely to be improved and may even be increased by massage vigorously applied. In cases in which these symptoms are marked only the gentlest frictions should as a rule be employed; these may diminish the spasm. Spastic muscles must be gently stretched by the hand; daily stretching does some good, but in cases with much spasm it is necessary to keep the muscles stretched continuously by means of a splint or to attempt to diminish the spasm by surgical means.

The most important part of the treatment of paralysis of the spastic type consists in the training of the muscles by exercises in order to re-educate control and co-ordination. The object is to put the joints systematically through their normal active movements, and it is essential to observe the position of neighbouring joints at the same time. For example, in spastic paraplegia flexion and extension of the foot may be voluntarily possible and may be carried out with fair accuracy if the knee-joint is flexed, but may be very difficult if the knee is kept extended. The muscles must be educated until all foot movements can be carried out voluntarily and accurately in all positions of the knee.

The training of a patient with spastic paraplegia in walking after the spasm has been relieved by such operations as tenotomy, nerve section, or posterior root section is a long and laborious business and may occupy two years or more. It involves education first in all joint movements taken separately and individually, then in standing with the knees and hips fully extended, first upon both feet, later upon each foot separately, then finally in the movements of stepping and walking.

In diseases such as tabes, in which the muscular sense is lost, re-education by exercises is again the underlying principle in treatment. Here the senses of sight and touch must be made to replace the sense of position which should be inherent in the muscles. The exercises most used are those devised by Fraenkel. In addition to simple voluntary movement of the joints, special exercises for the proper co-ordination of the legs and arms must be carried out. Lying down, the feet are moved at the word of command and placed in one of a number of slots in a notched board, walking is practised upon a floor space which is marked out with footprints into which the feet must be accurately placed. Then the patient is shown how to rise from a chair, first placing his feet back beneath the centre of gravity of his body, a movement instinctive in the normal person, but one which has to be learnt again when the sense of muscular position is lost. Finally, such movements as turning have to be practised. The arms must be exercised by seizing one of a number of fixed pegs, by fitting pegs into holes, by picking up and arranging small articles and similar exercises in co-ordination, the exercises being graduated so as to be increasingly difficult. Very great improvement in co-ordination may be thus secured in the majority of cases.

Diseases of the Thoracic Organs.—Improvement in the possible and in the habitual range of the respiratory movements is one of the most evidently advantageous results of well-designed physical exercises. Such breathing exercises, besides being useful in all sorts of general conditions of debility, etc., should be carried out as a routine in the treatment of deficient chest expansion co-existing with nasal obstruction, after operations for adenoids, in the subjects of frequent nasal and pharyngeal catarrh, and in those with kyphosis and flat chest. In chronic bronchitis and in asthma massage of the chest and abdomen is often advocated, and may in some cases be beneficial. It must, however, be carried out with careful supervision, and expiratory movements rather than deep inspirations should be practised.

After pleurisy, empyema or other conditions in which the chest expansion is asymmetrical, breathing exercises are important and, in fact,

almost essential. Unilateral movements in which the expansion of the sound side are hindered may be used.

In heart disease massage and graduated exercises are often useful; they should invariably be carried out under close medical supervision, as it is very easy to do more harm than good. It is impossible here to do more than briefly state the principles involved. General massage is sometimes useful by dilating arterioles and assisting the venous flow; it will often relieve an embarrassed heart, but it is easily seen that such a peripheral dilatation of the arterioles may in some cases do positive harm. Breathing exercises are again of service in assisting the circulation mechanically. Graduated exercises combined with the natural effervescent baths form the basis of the Nauheim treatment. The baths have a general stimulating effect upon the skin, which relieves the heart probably by producing dilatation of the peripheral arterioles. The graduated exercises are designed to increase the work of the heart slowly, and so to bring about a sufficient compensatory hypertrophy. Local massage over the heart is advocated in some systems of massage in the hope that it will stimulate the heart directly. It is very little used in this country, and in fact such direct stimulation of the heart, if it is possible, does not appear to be by any means necessarily advantageous.

Diseases and Injuries of the Joints.—In maintaining or restoring the function of a joint after injury or disease treatment by massage and movement finds one of its chief uses. In considering the principles upon which they must be applied it is necessary to differentiate clearly between massage and movement. Often both are advisable, but almost equally often it is necessary to employ massage whilst keeping the affected joint at rest. The simplest method of differentiating between lesions of joints that require rest and those that require movement is to act upon the old advice, "Rest all inflamed structures," bearing in mind that in modern pathology the reaction of the tissues to an aseptic injury is not inflammation, and that inflammation must also be differentiated from the subsequent period of organisation of the inflammatory products. In sprains and allied injuries the first object is to get rid of any effusion; massage with the assistance of a firm (compression) bandage will in most cases rapidly effect this. The second object is to restore the mobility of the joint; this is effected by movements. Throughout the treatment the nutrition of the muscles is maintained by massage, and as soon as they can be performed by active movements. The most difficult question to decide is the time at which movements should be commenced. It may be said at once that the presence of an effusion is no contra-indication, nor is the occurrence of a moderate amount of pain on movement. The only reason for withholding movements in the treatment of a sprain is the existence of a known injury to an important ligament, so that there is a risk of preventing its union and so leaving a weakened joint. This in most joints is an exceptional occurrence, and when it has occurred it contra-indicates movements in certain directions only, for with due care other movements can be carried out from the first. As soon as there is no risk of displacement of the joint, active movements and functional use of the joint are advisable, the joint being supported by strapping if necessary. Sprains thus treated by early movement recover rapidly. Excessive resting of a joint after injury is a prolific cause of periarticular adhesions, which in subsequent movements of the joint are pulled upon and stretched, leading to attacks of synovitis.

In acute or subacute arthritis due to some form of bacterial infection, massage may, if thought advisable, be carried out from the first, or at least as soon as the more acute symptoms have subsided and it becomes clear that the inflammation is about to subside without suppuration. But during this stage it is better not to attempt movements of the joint, in fact, fixation upon a splint is often desirable. In such a form of arthritis as that due to the gonococcus the best indication for beginning movements is the subsidence of the pain. It may be laid down as an axiom that attempts to move the joint during the early painful stage, by increasing the inflammation, will hinder the return of movement in the joint and may even lessen the movement that is subsequently restored. So that, as a rule, massage of the joint and of the muscles should be performed early, movements as soon as they are not accompanied by much pain, and the latter should always stop short of producing severe pain. If it is found that no progress is being made, it is better to examine the joint under an anæsthetic, some of the adhesions can thus be broken down, and at the same time information may be obtained as to the amount of recovery likely eventually to result. In tuberculous arthritis it is hardly necessary to say recovery of movement must be spontaneous, it is never allowable to attempt to obtain it manually, although massage of the muscles is a perfectly correct treatment.

In osteo-arthritis and in old-standing rheumatoid arthritis comparatively little benefit is to be expected from treatment by massage and movement, unless there has been a neglect of all endeavour to retain mobility in the joint during the earlier stages. In more recent rheumatoid arthritis, however, very great benefit may result

from appropriate treatment, but it is necessary to bear in mind what has already been said about attempting to force movement in an inflamed and painful joint. First, the more acute progress of the disease must be arrested; active and passive movement may then be used with benefit.

Fractures.—Great misconception exists as to the uses and limitations of massage and movements in the treatment of fractures. These methods can only be accessory to the other methods of treatment, but they are accessories that cannot in the interests of the patient be ignored. In order that the limitations of their employment may be understood, it is necessary to allude briefly to the reduction of displacement and to the splinting of fractures. Displacement of the fragments in a fracture may be caused by the force which produced the fracture, or it may be the result of the pull of muscles, or of the weight of the limb. If the first named be the sole cause, as it is, for example, in Colles's fracture, there is no tendency to the recurrence of the displacement when this is once reduced; if the second or third causes are concerned there may be a tendency to such recurrent displacement, and this may have to be guarded against by a splint or by an extension. The chief limitation to the employment of massage and movement in the treatment of fractures is that necessitated by this tendency to recurrent displacement. This must be analysed in each case. In Colles's fracture there is no tendency to recurrence, massage may be employed from the first, and the splint may be removed in order that it may be carried out. In Pott's fracture the splint may be removed for massage at the end of a week; in practically any fracture, including that of the shaft of the femur, the splint may be removed for a massage at the end of three weeks. The object of the early massage is to assist absorption of effusion, and it is obviously desirable to begin this portion of the treatment as early as possible—that is to say, as soon as the part can be got at. The question of movement is less simple. It is necessary to insist that by movement we mean normal joint movement, and not movement of the fractured ends of the bone upon each other. Such normal joint movements may with advantage be carried out as soon as there is no risk of producing displacement. They must be gentle from the first, never pushed to the extent of causing much pain, and any movement which might displace the fragments must be avoided; for example, in a Pott's fracture, flexion extension and inversion of the foot may be commenced early, eversion of the foot should be left until after about three weeks. It is specially necessary that all massage and movement in the treatment of a fracture should be gentle. Massage aids the formation of callus; if carried on vigorously, particularly if accompanied by vigorous attempts to force movement, the callus may be produced in an amount that becomes embarrassing. The production of excessive new bone around the elbow after a fracture of the lower end of the humerus is undoubtedly partly, if not entirely, due to too-vigorous treatment by massage and movement, and the complete cessation of the treatment will usually suffice for its cure. In the method of treatment of fractures by massage identified with the name of Lucas Championnière, the necessity for gentle treatment is specially insisted upon. This French school also use repeated centripetal stroking of a limb as an analgesic; it is stated that by this means in the course of a few minutes the area of a fracture may be rendered practically anæsthetic, so that muscular spasm is relaxed, and a recent fracture if not impacted may be reduced without pain.

Spinal Curvatures.—The treatment of spinal curvatures, kyphosis, lordosis and scoliosis, by exercises has been elaborated into a system, or rather perhaps systems, of considerable complication. It is only possible here to allude briefly to the principles of treatment and to its limitations. All spinal curvatures are capable of classification into postural curves, in which the spine is anatomically normal and can be restored by the patient's own muscular effort to a good shape, and structural curves, in which there is a structural deformity of the spine, usually in the vertebræ, but sometimes in the muscles, so that the patient cannot by his own muscular effort attain a proper posture. In the first class of case the treatment is purely a muscular problem; a properly designed system of exercises is capable of effecting a cure. In the second class of case exercises are only subsidiary to other forms of treatment. By themselves they may prevent any progress of the deformity, but they cannot completely cure it, the most that they can do is to enable the patient to maintain such a posture as will hide the deformity. This is often all that can be promised by any method of treatment.

In drawing up a table of exercises for a patient suffering from a spinal curvature all the points already alluded to must be borne in mind. The table, with massage at the end, will last, as a rule, from forty minutes to an hour. It should begin with breathing exercises and a few plane arm movements, include a considerable variety of exercises, which must be changed from time to time so that they do not become monotonous, and should end with more breathing exercises and massage of the back muscles. The principles that have to be borne in mind, are—

1. That the first essential is to train the

patient to maintain her best posture, at first as the result of directions, later of her own accord. So that the first essential is that the instructor should see that the initial position from which exercises are carried out is correct.

2. That control of the muscles must be obtained. At first the patient finds it difficult to carry out the movements accurately at the word of command and requires assistance. She gradually, however, attains more complete command over her own muscles.

3. The strengthening of the muscles in general or of particular groups is the third requisite. This is, however, less important than the improvement of muscular control.

4. In structural curves correction of the more fixed part of the curve by manipulation with the hands or with straps, or by stretching over the boom, is desirable.

The carrying out of exercises for the treatment of a spinal curvature is a matter of considerable difficulty, and the instructor must be carefully chosen. Exercises to improve posture and control of muscles will not effect their object if they are carried out in a slovenly way however well they may be designed. Exercises which are intended to strengthen muscles are even more difficult. If badly designed and carried out they may easily make a curve worse. It is, in fact, a common occurrence to find that a patient by vigorous exercises has been made considerably more deformed, or at least that the curve has been made more fixed.

R. C. E.

TREATMENT BY HYPNOTISM, SUGGESTION AND PSYCHO-ANALYSIS

The two chief methods of treatment in use at the present time which depend for their results on their influence on the mind of the patient are suggestion, with or without hypnosis, and psycho-analysis. The rôle of the two methods is entirely different, and while many of the neuroses may be benefited by either used separately, a number can be best alleviated by a combination of the two.

I.—The method of **Suggestion during Hypnosis** is that mainly used in this country.

The chief characteristic of the hypnotic state is increased suggestibility; and this is seen in every stage from the lightest hypnosis to the deepest sleep. But increased suggestibility is not the only phenomenon characteristic of the state. An obvious loss of spontaneity is usually to be observed, especially in the later stages, the subject remaining motionless except when carrying out a suggestion. Marked loss of memory distinguishes a subject aroused from the deepest stage, he being quite unable to recall the events of his hypnotic sleep.

The subject is not only more susceptible to suggestion in hypnosis, but is able to realise the idea suggested with an intensity quite impossible in waking life. Thus, if a lady in the normal state is told that her dress is on fire, she will accept the suggestion to act accordingly; but, when she sees that the suggestion is false, she will no longer act on it. If, however, she be hypnotised, she will both act in accordance with the idea, and will really see the smoke and flame, and so become subject to an hallucination. Many of the phenomena induced by suggestion occur spontaneously in other abnormal conditions. Such are the anæsthesias and paralyses of the hysteric, and the stigmata of certain religious devotees, etc.

The different stages of hypnotism can be distinguished by the particular groups of suggestions which can be enforced in each.

(*a*) **Stages.**—In the first stage, one of the phenomena most easily induced is inability to open the eyes. Heidenhain pointed this out many years ago, and stated that in many subjects it was the only sign that could be elicited —and I fully concur with him. It appears that in the *first stage* all one can do is to inhibit those actions which are usually carried out reflexly, though by voluntary muscles. Such are the movements of the eyelids, swallowing, breathing and micturition. Sneezing, which is a purely reflex act, though carried out by voluntary muscles, can be inhibited whether the subject be hypnotised or not. Thus practically no one, when told that, when he takes a pinch of snuff or pepper, he will be unable to sneeze, can do so.

In the *second stage*, ordinary voluntary movements can also be inhibited. For example, the patient is unable to loosen an object when told he cannot, or drop anything which he holds in his hand, though it is easier to prevent him from dropping a heavy than a light object. He cannot pass a line drawn on the floor; he cannot get up, and even cannot speak if silence be suggested. It is during this stage that so-called contracture or muscular rigidity can first be induced. The limbs are stroked, and the suggestion is made that they are stiffening. The subject is quite unable to relax his muscles until that suggestion is removed. Possibly the initial inability to open the eyes is due to contracture of the orbicularis oculi muscle. He cannot perform actions, sometimes because he feels under a strong disinclination to try, sometimes because he cannot make up his mind to do so. More commonly, however, he can and does try; and, though he contracts the appropriate muscles, he is obliged to contract their opponents so strongly that he cannot achieve the forbidden action. Thus, if he is

told he cannot loosen the operator's hand, when he tries to do so, he will grasp it more firmly instead.

In the *third stage* imperative suggestions begin to take effect, and the subject can be compelled to begin and to carry out an action. He can be made to laugh, to get up, or in fact execute any desired movement.

In the *fourth stage* he can usually be induced to forget any selected fact. Thus he cannot recollect his own name if told he cannot. Local analgesia can also often be induced, and semi-hallucination also. For example, a paper-knife held in the hand may be made to seem so heavy that it drags the holder to the ground, and so hot that he must throw it down.

In the *fifth stage* visual and auditory hallucinations can be induced; but the memory is intact, or nearly so, on the awakening.

In the *sixth stage* all the phenomena of the previous stages can be evoked; but the memory of the events occurring during this stage is abolished on awakening, though it may be revived during subsequent deep hypnotic states. The condition in this stage is often termed somnambulism.

It is in this stage that what are known as post-hypnotic suggestions can be most effectually made, and from a therapeutic point of view they are of great importance. If during somnambulism a patient is told that at some time after he awakens he will do a certain action, he does it as suggested. But he is utterly unaware on awakening that any such suggestion has been made, and, as a rule, when he carries it out, believes the action to be done of his own free will.

It is interesting to notice that by persistently assuring the patient that he can remember what happened during his sleep, he can often be persuaded to recall the events partially or completely. It was this phenomenon that first turned Freud's attention to the possibility of making patients recall long-forgotten episodes, which led to the discovery of Psycho-analysis.

It will be seen from the above brief account that the popular idea that the subject becomes "unconscious" during hypnosis is entirely false. At all stages, even the deepest, he is acutely conscious. The notion has probably arisen from the amnesia which follows the sixth stage. It appears to be a peculiarly mischievous idea in practice, many patients insisting that they have not been hypnotised because they were fully conscious the whole time.

The results of hypnosis vary greatly with different individuals. Some show the phenomena at the very earliest stages, and while many show the phenomena of the first three or four stages, only about twenty per cent. pass into the sixth. I may here note that a few subjects show the phenomena of the second stage before those of the first; but these are quite exceptional.

(*b*) **Theories.**—There is, so far, no completely satisfactory explanation of the phenomena of hypnosis. On the physiological side, the theory of dissociation, which has been ably advanced by Dr. McDougall (*Brain*, July 1908) seems the best proposed, although purely speculative. It assumes variation of resistance in the different neurones during hypnosis which cause alterations in the direction and amount of the flow of neurokyme or nerve energy.

On the psychological side various theories have been advanced, largely founded on the changes of memory—or rather the loss of memory—on awakening from somnambulism, its recovery during subsequent hypnoses, and also on the curious phenomena of motor and sensory automatisms. Most of them suppose that a disintegration of consciousness takes place, the total consciousness being partially or completely split into two—the waking consciousness and the subconsciousness, the subconsciousness alone being affected by suggestion. It is, however, doubtful whether the term subconsciousness is not really a misnomer, and whether "the unconscious" does not come nearer to reality. Munsterberg considers that the "subconsciousness" has no existence, and that the phenomena attributed to its activity are simply automatic processes, analogous to the automatic playing of a practised musician, in which consciousness has no real part. It is a conception not unlike that of Carpenter's "unconscious cerebration."

But as a working hypothesis the fundamental idea of a split-off consciousness is extremely useful, even though it may not be absolutely accurate. However, the problem is still unsolved. Hypnosis, then, may be regarded as a condition of artificially induced suggestibility. Sidis has laid down the following conditions as necessary for the induction of the state—

1. Fixation of attention.
2. Monotony.
3. Limitation of voluntary movements.
4. Limitation of the field of consciousness.
5. Inhibition (*i. e.* the inhibition of all extraneous ideas).

Of these the essential condition is the fourth—limitation of the field of consciousness; the rest are merely useful in securing it.

One may suppose that concentration somehow causes the consciousness to split into two paths. This is seen in a slight degree in the phenomenon known as passive attention. A man engrossed in conversation, walking in a crowded street, does not collide with his fellow passengers, but avoids them. Yet this avoidance may

be almost entirely unconscious. His "passive attention" has been brought into action by his mental absorption, forming a kind of protective mechanism, and we may suppose that the action is in some degree subconscious. At any rate there is no doubt that mental concentration does result in increased suggestibility.

(*c*) **Methods.**—Numberless methods may be used based on this principle. Personally I generally use one which is designed to prevent, as far as possible, any conscious resistance on the part of the subject. The patient is told that he really hypnotises himself, and that all any one else can do is to help him in the process. He is impressed with the idea that the essential point is the concentration of his attention. I tell him to fix his attention as much as he can on some small object held about eight or ten inches from and slightly above his eyes. He is told to blink as much as he likes, and to let his eyes get as heavy as ever they will, not to rouse himself on any account, but to sit motionless, with all muscles as relaxed as possible. After a few seconds the forehead is quietly stroked, and suggestions are commenced, such as, "Your eyes are feeling heavy already. They are beginning to close," etc. In a very short time, as a rule after less than two minutes, the eyes close. I now lay my hand firmly on the patient's forehead and say, "Your eyes are fast—you cannot open them, you may try as much as you like"; and it is quite rare for a patient to do so.

As might be expected, patients may at first find difficulty in concentrating their attention and preventing the entrance of extraneous ideas; and, until they can, each trial for hypnosis is a failure. Hence, if hypnosis cannot be induced the first time, they must be trained in concentration. Success can almost always be assured after a few trials if this discipline is carried out.

Once the first stage is reached, even if no deeper hypnosis is possible, therapeutic suggestions may be commenced.

This initial phase being induced, attempts may be made to deepen the hypnosis, both by suggesting the phenomena of the stages in their proper order, and by the reiterated suggestion of sleep. Even though no sleep be induced, this suggestion tends to deepen the condition.

Increased suggestibility for therapeutic purposes may be induced by other methods than hypnosis.

(*d*) **Hypnoidal State, etc.**—In the hypnoidal state, first described by Sidis, the patient becomes sufficiently suggestible for therapeutic purposes, though perhaps not so much as in hypnosis. The hypnoidal state is intermediate between the state of waking and that of normal sleep: it is unfortunately, but naturally, often very transient. It can be readily induced by any means which will cause sound sleep. The patient may lie with his eyes closed in a darkened room, and some monotonous sound such as the beating of a metronome, the ticking of a watch, or the sound of running water, will usually suffice to bring it about. The breathing becomes slightly irregular, and the patient resists and resents any attempt to move his limbs; I have also noticed slight spasmodic movements of the limbs.

Therapeutic suggestions given in this state are often highly successful. Bramwell's method of giving suggestions in a monotonous tone of voice, while the patient rests with closed eyes, and attends, not to him, but to some restful train of thought, depends probably for its success on the occurrence of the hypnoidal state. Altogether, this mode of treatment is useful for patients who decline to try hypnotism, or who are insusceptible to it, for it consists simply in making suggestions in the normal waking state.

It may be pointed out that the mechanism called into play is entirely different to that acting in hypnosis. The suggestion merely persuades the patient to look at his complaint from a rational point of view, so that by his own reassurance he may break away from his morbid condition. Hypnotic suggestion, on the other hand, makes no appeal to his rational self, but only to his subconsciousness. In treating by the hypnoidal method, the aim is to get the patient to understand his illness and its causes—a rather difficult matter if the physician himself happens to be at a loss as to what they are.

It is also necessary that the patient should be intelligent enough to understand the purpose of the treatment. In addition, the physician must be a man of unlimited patience and great powers of persuasion. The treatment is, therefore, only useful in a limited number of cases, but in these the results appear to have been excellent.

II.—Psycho-Analysis

The method of treatment elaborated by Prof. Freud of Vienna is applicable to many cases of psychoneurosis. But it must be clearly understood that its scope is distinctly limited. It is of no use in early childhood or old age; it requires from the sufferer great patience, an intelligence at least equal to the average, and, what is rare in the English at any rate, the power of casting away all reserve whatever, while from the physician it demands at least an equal patience and rare gifts of psychological penetration.

According to Freud's theory the psycho-

neuroses have their origin in ideas combined with emotion, forming what are called complexes, which complexes exist, not in the normal consciousness, but in what Freud terms the "unconscious." These systems of ideas acting apart from, and often in antagonism to, the waking consciousness, induce the symptoms of the various neuroses, *e. g.* phobias, imperative ideas, paralyses, etc. They are the result of unfulfilled "desires" existing in the unconscious. But if the complex causing the symptoms be slowly illuminated, and the patient made to realise and recollect its origin, the symptoms vanish, sometimes at once, more often gradually. The process of unearthing the complex is called Psycho-analysis.

As before stated, it is possible to get hypnotic subjects to recall the events occurring during somnambulism by repeatedly insisting that they *can* remember them. By a similar process Freud found that he could sometimes get patients to recognise what the complex was that caused their symptoms; and since then other methods have been devised for the same object, especially the method of "free association," and the interpretation of the patient's dreams.

Under "free association" the patient lies at rest, fixes his attention on some fact connected with his illness, and observes the ideas and images which present themselves to his mind. He must simply observe, not criticise in any way, lest the ideas be influenced by his mental attitude, though naturally it takes a little practice before he can do that. Each image as it arises he watches intently, and describes minutely to the physician, who firmly insists that ideas of some kind must rise up to his vigilant and waiting consciousness.

His dreams also he must try to recollect and describe with equal minuteness. The images of dreams are always symbolic in adults, and Freud, in his work on *The Interpretation of Dreams*, gives a number of symbols, the meaning of which his vast experience has enabled him to determine.

Other methods there are, notably that of Jung, in which a list of words is read to the patient, he uttering the first word that occurs to him as each is read. Partly by the reaction time, by the response-words given by the patient and in about ten other ways, hints are obtained which may serve as beginnings for fresh trains of analysis.

As a rule, the patient must be seen for about an hour at a time. By constant questioning, and insistence that the subject *can* remember, with the aid of the interpretation of his dreams, and the images and ideas aroused by free mental association, the complex is gradually reached, and eventually completely unmasked.

In every case, according to Freud, there is a sexual basis for psychoneurosis, though many disagree with him. He goes so far as to state that with a normal sexual life psychoneurosis never occurs, so that the aim is really to determine the actual sexual trauma which is at the base of the symptoms. The process is a very long one, lasting months and sometimes years.

It appears to me that it is not suitable for trial in many cases, as no one would wish to suggest unpleasant and revolting sexual ideas to those in whom they do not exist. But when there is a strong probability that some sexual shock lies at the root of the mischief, there cannot be the same objection. Even then, however, it would seem unlikely that it would be possible to break down the reserve of the average Englishman, and an intentional refusal to give the details, often repulsive details, is an absolute bar to success in a task already rendered difficult by the *unconscious* resistance of the patient as he or she becomes dimly aware of the nature of the neurotic symptoms.

III.—Maladies Amenable to Suggestion

In treating patients by suggestion, it is found that, although the results may be more rapidly obtained in the deep states, the very lightest hypnosis is often sufficient.

Suggestion may be successfully used in treating other than purely mental disorders; constipation, dysmenorrhœa, metrorrhagia, amenorrhœa, hyperhydrosis and other functional complaints have been successfully treated. Forel gives the following list of complaints to which it is especially applicable—

Spontaneous somnambulism, pains of all descriptions, insomnia, functional paralysis and contractures, organic paralyses and contractures (as palliative means), chlorosis, disturbances of menstruation (metrorrhagia and amenorrhœa), loss of appetite and all nervous digestive disturbances, constipation and diarrhœa (provided that the latter does not depend on catarrh or fermentation), gastric and intestinal dyspepsia (including pseudo-dilatation), psychical impotence, nocturnal emission, masturbation, perverted sexual appetite and the like; alcoholism and morphinism (only by the suggestion of total abstinence), chronic muscular and arthritic pains, lumbago, the so-called neurasthenic disturbances, stammering, nervous disturbances of vision, blepharospasm, pavor nocturnus of children, sickness and sea-sickness, and the vomiting of pregnancy, enuresis nocturna, chorea, nervous attacks of coughing, hysterical attacks and bad habits of all kinds. All hypochondriacal paræsthesias, irritable weakness, conceptions of impulse and the like are more difficult to treat.

It must not be supposed that the above list is necessarily exhaustive. Some of the complaints given, too, will often yield to analysis, or analysis combined with suggestion, but may be quite unamenable to suggestion alone. Such are functional paralysis and neurasthenic and hysterical disturbances.

But many are eminently suited to hypnotic treatment alone. Of these I may mention a few of the commoner and more important.

(*a*) **Insomnia.**—Whilst hypnotism often cures cases of chronic insomnia, it is generally quite useless in an emergency case, where it is important to induce sleep immediately, unless the patient happens to have been hypnotised on some previous occasion. In chronic cases the results are often good. The patient must, however, usually submit to a regular course of treatment, though occasionally I have found a single hypnosis sufficient to cure permanently a disease of long standing, in one instance the case being of seven years' duration.

(*b*) With **Alcoholism** in most of its forms, suggestion is eminently successful.

The three chief forms of this disease are: true dipsomania—a comparatively rare disease—pseudo-dipsomania, and chronic alcoholism.

In *true dipsomania* the attacks of craving are independent of the taking of alcohol, and occur even during periods of total abstinence. As a rule the attacks are heralded by premonitory symptoms which last a week or more, and the ensuing debauch of alcohol endures a few days, after which the frenzy ceases, often leaving the patient very ill for a little. In course of time the next attack occurs, exactly in the same way. Very few of these patients can drink in moderation between the attacks: some, however, can, being apparently perfectly normal until the attacks happen. I do not believe that hypnotism has the slightest effect on these cases. The attacks can, however, be satisfactorily treated on the lines laid down by Dr. Francis Hare.

In *pseudo-dipsomania*, the patient remains free from any attack for an indefinite time, the collapse arriving only if he takes alcohol. Usually a single glass will ensure the occurrence of a drinking bout. In the majority of these cases, alcohol produces depression after the first stimulating effects have gone. The time in which depression develops varies enormously. With one patient it occurred always within twenty minutes of taking the first glass. In another it did not come on for nearly thirty hours. The craving in these cases consists in a desire to escape from the feelings of misery; and alcohol immediately relieves the patient, only to plunge him again into the same condition later. Some have told me that the reason they did not stop was that they dared not. Many dislike the taste of alcohol extremely during an attack; but that is no obstacle to their taking it. As a rule, after a few days—a week or more—the patient suddenly ceases to drink, often because his stomach is too much upset for him to go on. The amount these people will consume is astounding. Three bottles of whisky a day is not unknown, and one patient whom I saw took no fewer than four.

In *chronic alcoholism* the patient drinks in excess quite regularly; I should say the average amount taken by such a case is one to one and a half bottles of whisky a day. Any sudden diminution after a long period of chronic alcoholism is liable to lead in a few hours to delirium tremens. I am convinced by experience of the correctness of Dr. Hare's contention that sudden withdrawal is exceedingly dangerous and liable to cause most alarming sequels. It is, I think, certain that in the cases on which the opposite view is founded the habit had been of short duration, in dealing with which total withdrawal is generally perfectly safe.

In treating alcoholism by suggestion the first essential is absolute abstinence from all intoxicants. This may be insisted upon immediately in the attack of the pseudo-dipsomaniac. With the chronic alcoholic matters must be contrived very slowly and cautiously. After the alcohol has been stopped, for which purpose the patient is much better left in bed, suggestive treatment may be begun. In my experience all alcoholics, except those whose condition is due to head injury, are readily hypnotised.

The suggestion in all cases must centre on making the patient a total abstainer, and strengthening his will power, special emphasis being laid on the absolute necessity of never again taking a first glass. Suggestion of increased self-control and terror of alcohol are useful; the latter I have found in several cases acting so as to prevent the fatal taking of the first glass in a casual way.

There are two other forms of dipsomania which I think deserve special mention, viz.: *menstruation dipsomania*, occurring in women only at the periods; *dipsomania due to insomnia*.

The first is often associated with irregular menstruation, and depression at the periods, the patient feeling that she must have something to "pick her up." It is possible to render menstruation regular in some of these cases, and to limit its duration exactly, and also largely to combat the depression. These cases may do exceedingly well: out of four cases of the kind only one relapsed, the rest having been free from any attacks since treatment, two for five years and one for three and a half years.

The insomnia cases are specially interesting,

the cure of the insomnia resulting at once in the cure of the dipsomania, some of these patients being the only ones I have met who can afterwards drink in moderation, becoming apparently absolutely normal.

Authorities differ as to the time during which an alcoholic patient should be under treatment. Personally I generally see my patients every day for eight days, twice during the ensuing week, once the week after, and then, if possible, regularly at long intervals of a month or six weeks for an indefinite period.

It must always be borne in mind that all these cases are liable to relapse, for there is no possible cure for the original nerve condition. And it is here that the chief advantage of the treatment comes in. A few days' treatment after a relapse will usually suffice to keep the patient safe for a still longer period; and though in some cases relapses may occur again and again, the patient has long periods between during which he can enjoy his life, instead of being almost constantly under the influence of the drug.

(*c*) **Morphinomania.**—As with alcohol, the first thing is to stop the taking of the drug. This must in all cases be done gradually if the habit has persisted for long. It is only the last grain or so which it is so difficult to give up; and the time required for this renunciation may be very prolonged. Thus, in one case of twenty years' standing, it took six weeks to leave off the last grain, the dose being diminished by one forty-eighth of a grain each day. But after the drug is given up there is for a long time great risk of the patient's beginning to take it again; and though suggestion answers in many of these cases, if they are not treated for some two, or even three, months, they usually relapse.

With regard to cocaine, I fear that treatment is practically useless. A confirmed case is hopeless.

(*d*) **Bad Sexual Habits.**—With young children, under twelve, the result of a single suggestion is, as a rule, immediate and complete, the habit ceasing at once. In adults the cure takes much longer. It is important to insist in these cases that the only possible way a patient can fight this particular vice is to govern his thoughts, and never allow himself to dwell even for a few seconds on sexual matters. One can give him power by suggestion to turn his thoughts away at once, and the cessation of the habit follows spontaneously.

(*e*) **Impotence** in the male, if of psychical origin, can frequently be cured, even after a duration of years. The idea causing the impotence must be sought for and counteracted, and for this purpose psycho-analysis is often essential. However, even if the idea be unknown, mere suggestion may be sufficient.

(*f*) **Absence of sexual desire,** and primary vaginismus in the female may be cured. The latter especially is, as a rule, quite amenable to suggestion.

(*g*) **Dysmenorrhœa,** especially of the so-called spasmodic type, I have seen vanish at once after many years' duration.

Prolonged and irregular menstruation also can often be regulated to the exact day of onset and cessation, especially if somnambulism can be induced.

(*h*) **Hysteria.**—These cases differ enormously in the degree to which they respond to suggestion. In some the symptoms vanish at once; in others not at all. These cases are really best treated by some process of psycho-analysis, either by itself or in combination with suggestion. In neurasthenia, analysis will frequently relieve the symptoms when other methods fail.

In hysteria there is often a considerable difficulty in inducing hypnosis of even the slightest degree. Hysterical subjects are often extremely self-suggestive—a condition highly unfavourable to hypnosis. It is in these cases especially that analysis has proved so useful. But the method is so tedious, treatment lasting for months and even years, that it is for most of us, except in quite rare cases, almost impossible, and in the view of many it is more than doubtful whether its advantages are not outweighed by the detailed sexual analysis which it involves. But it is possible by a partial analysis in many cases to gain sufficient knowledge of the ideas causing the symptoms without going deeply into sexual details.

Thus, in one patient who was unable to go out alone, because she was seized with terror if she did so, the unconscious idea causing the terror was that she would go mad, and that the people in the street would seize her and hurry her off to an asylum. Suggestion removed the idea at once; and the fear vanished. But according to Freud there would be found a sexual basis for this idea, if analysis were completed. There may have been, but I never attempted to discover it, and it appears to be unnecessary to do so, in some cases, at all events.

Cases of obsession, melancholia and sometimes imperative ideas (though often these are very stubborn) may be benefited, as well as the various phobias.

(*i*) **Complaints not Definitely Mental in their Nature.**—Of these *Constipation* is the most typical, and can often be permanently cured. Cases of lifelong constipation may yield to suggestion; I have seen one of fifty-three years' standing completely and lastingly relieved. The suggestion should be made that the bowels will act at a specified hour. Even if a daily evacuation cannot be obtained, it is often

possible to obtain one every second or third day.

Menstruation, as mentioned previously, can often be regulated exactly; and the pain of spasmodic dysmenorrhœa obviated.

Chorea will sometimes vanish almost immediately.

Some cases of *Eczema*, presumably of nervous origin, are reported to have been completely and rapidly cured.

Nocturnal Enuresis often yields; but is very uncertain, for many cases fail to improve. It occurs often in such deep sleep that the patient is apparently beyond the range of suggestion.

With *Stammering* in young persons of fifteen or under the results are very good, and success is often obtained in adults. I have found self-suggestion very useful with these patients.

Attention must be paid to the cause of stammering, *e. g.* wrong breathing, etc., if it can be discovered. Some cases occur after whooping cough, and these I have failed entirely to improve.

Forel states that the results in *Chlorosis* are extremely good. The hypnotic sleep without suggestion is said to be beneficial.

In *Asthma* the results during an attack are almost magical, and I have seen a fair number of cases in whom self-suggestion can be most effectively used. The results are not, as a rule, permanent; but the attacks can usually be shortened.

Sickness and sea-sickness are generally easily preventable, and the vomiting of pregnancy is said to be relieved. Suggestion has, of course, been used as an anæsthetic; but since the introduction of physical anæsthetics it has naturally fallen into disuse. As a rule the patient must have had some previous hypnotic training. The anæsthetic value of suggestion is still useful for the removal of pain, such as that of headache or neuralgia, and is, I think, specially suitable for confinements.

H. E. W.

TREATMENT OF TUMOURS BY DIATHERMY CAUTERY

The apparatus required for Diathermy consists of a motor which produces a high-frequency current of great power and two electrodes, a large one which is wrapped in wet towels and laid on the patient's chest or abdomen, and a smaller one which has a metal end which can be applied to the tumour. The passage of the strong current through the small electrode, or cautery, produces intense heat which rapidly destroys the tissues. On the other hand, very little heat is produced in the region of the larger electrode because of its greater size.

By diathermy it is possible to destroy any amount of tissue, but care should be observed that the sloughs produced are not too large, otherwise there may be septic absorption or bleeding if a large artery lies in the immediate neighbourhood of the wound.

Treatment is carried out in the following manner: A general anæsthetic is required. The growth must be sponged until the surface is quite dry. The small electrode or needle must be plunged into the growth so that all the metal is covered. The current is then turned on and in five to ten seconds the tissues around the metal are completely destroyed. As soon as the parts become white, or when bubbles appear on the surface of the tumour, the current must be switched off. By a series of similar punctures every part of the growth can be attacked. The operation can be completed in about five minutes. Even with vascular tumours bleeding is very slight, but the surface of the growth requires frequent sponging to keep it dry.

Diathermy for Malignant Growths.—The author has treated cases of inoperable carcinoma with this method during the last five years. The growths have involved the palate, tonsil, base of tongue and pharynx, and were associated with urgent dysphagia, blood-spitting and constant expectoration; many of them were considered too advanced for operations with the knife. There has been very little pain even after extensive destruction of tissue, and the patients could swallow well in twenty-four to forty-eight hours. It is remarkable that the surrounding tissues do not become much inflamed, and there appears to be no tendency to œdema such as occurs with milder forms of burning. The sloughs produced by diathermy separate in five to ten days, leaving a healthy wound without discharge. In many instances the ulcer disappears and the parts are covered with soft mucous membranes. When the whole of the growth has been destroyed there is no tendency to scar formation, as frequently occurs after other operations. There has been no shock, and the patients have only been confined to bed for twenty-four hours. Secondary hæmorrhage has not occurred and there have been no other complications except slight burning in the region of the larger electrode. In most cases more than one operation was found to be necessary.

All the patients were definitely improved by the treatment. The best result was obtained in an old man with a growth on the front of his tonsil and adherent to the upper and lower jaws. Seven applications were made, and he lived for two years after the first application.

In most of the cases improvement was only temporary, but the patients were relieved of severe pain and were able to swallow more

easily. In one case of carcinoma of the cheek it was found possible to excise the growth some weeks after the application of diathermy. In two cases the primary ulcer was destroyed by burning and cervical glands were removed by a second operation. In another instance radium treatment was also given and the patient was definitely improved.

There appears to be no difficulty in destroying the superficial parts of these diseases and the throat is more comfortable afterwards. There is no evidence to show that the cancer cells are more easy to kill than normal tissues. It is possible that there is less tendency to recurrence than after a cutting operation, because the blood- and lymph-vessels are sealed by burning. In some of the cases where growth remained, it became atrophic in character. Diathermy is also valuable for the treatment of early growths, but it is yet too early to say whether the method will give as good results as the knife in this or other parts of the body. The obvious advantages are the rapidity of the operation and the possibility of destroying a dangerous growth without the loss of a single drop of blood.

Diathermy for Nævi.—Vascular cavernous nævi of the tongue, pharynx, nose and in rare instances of skin, can be safely treated by diathermy. The heat developed by the instrument is so intense that there is no tendency to bleeding. Secondary hæmorrhage does not occur even when a part only of the nævus has been treated.

Diathermy may also be used in rare instances for other conditions, such as lupus of the mucous membranes of the upper air passages, for destruction of enlarged or septic tonsils, or for removal of innocent neoplasms.

W. D. H.

SPECIFIC THERAPY

The object of specific therapy is to promote the patient's recovery from a given infection by raising his resistance to the particular pathogenic micro-organism by which he is being attacked. It has been shown that recovery from a bacterial infection depends in no small degree upon the ability of the patient to put forth and maintain a sufficient supply of specific antibodies. The aim of specific therapy, therefore, is to increase the patient's fund of specific antibody. For this purpose three practical methods are at present available, viz: (1) Vaccines; (2) immune serums; (3) sensitised vaccines.

Vaccines.—A vaccine consists of a suspension of a pathogenic micro-organism either attenuated or killed. In certain special instances, *e.g.* tuberculin and mallein, the bacterial bodies are disintegrated and a solution of their contents is used. In either case the active principle of the preparation is the endotoxin of the bacterial bodies. The first step in the preparation of a vaccine is to obtain a pure culture of the micro-organism. In the majority of instances, *e.g.* in case of staphylococcus, streptococcus, pneumococcus, gonococcus, M. catarrhalis, meningococcus, B. coli, B. typhosus, B. pyocyaneus, etc., a young culture on agar is suitable. It is advisable to use a strain recently isolated from the body, and when possible the patient's own micro-organism is preferable; in which case the vaccine is said to be autogenous. As it is impossible to make an autogenous vaccine in every case, stock vaccines are made in most hospital laboratories by mixing several strains of the same micro-organism and keeping the mixture in stock for use as required. Having obtained a suspension in saline of a young culture of the organism, the next step is to standardise the vaccine by determining the number of bacterial bodies in a given volume. This may be effected by one of several methods. In the procedure devised by Wright a measured volume of the suspension is mixed with a volume of blood and after thorough admixture film preparations are made, stained, and the number of bacteria and red corpuscles respectively counted in a series of fields; the number of red corpuscles in a cubic millimetre of blood being known, it is easy to find the number of bacteria in the saline suspension by this method.

A second method of standardising a vaccine is to mix a volume of it with an equal volume of a dilution of some stain such as methylene blue, and then to count the number of bacterial bodies that deposit from the mixture over the squares in a Thoma-Zeiss counting chamber. Other methods are also available. It is usual to label vaccines by the number of bacterial bodies that they contain per cubic centimetre.

Mode of Sterilising the Vaccine.—Vaccines are killed either by heat, in which case a temperature at or about 60° C. is generally used, or by an antiseptic such as phenol, lysol or ether, or by autolysis. In the last case all that is necessary is to put a suspension of the organism in saline into the incubator at 37° C., and to leave it there overnight. Provided the emulsion is not too strong, a subculture on the following day will show that the micro-organism is dead.

Keeping Capacity.—Vaccines should be kept in a cool place and in the dark. It is advisable to seal them off from the air. Though they may be active after being kept for a year or more, it is generally advisable to use them within a few months of their preparation.

Mode of Administration.—Vaccines are given in nearly all cases subcutaneously. The site at

which they are injected is immaterial, the loose tissue on the extensor aspect of the forearm, or the arm, or the flank are equally suitable.

Dosage.—This varies according to the condition of the patient and the kind of organism in use. The rule is to begin with a small dose and gradually to increase it unless the patient gets a "reaction." A reaction may be either local or general, or in the diseased area. In the first case there is some redness and œdema at the site of inoculation. A general reaction is characterised by malaise and a rise of temperature; in severe cases there may be a rigor. When there is a reaction in the diseased area there is some slight aggravation of the local symptoms. The reaction is produced by too large a dose of the vaccine, and it may come on at any period from half an hour up to forty-eight hours after the injection. Although there is as a rule marked improvement after it has passed off, the reaction is better avoided, and this can be effected by beginning with a low dose and by not raising it too rapidly. As a rule much smaller doses of vaccine should be used in acute cases than in chronic. In most cases 1–5 millions is a suitable dose to begin with, but in cases of boils or acne in which Staphylococcus vaccine is used, it is safe in most cases to begin with an initial dose of 50–100 millions. In an ordinary case doses of vaccine may be given once a week.

Modus Operandi and Choice of Cases for Treatment.—The object in giving a vaccine is to promote the formation of antibodies by the body cells. Thus, in the case of a person suffering from boils on the back of the neck, the introduction of a suitable dose of staphylococcus vaccine under the skin of the forearm appears to cause first a small fall in the amount of circulating antibody (negative phase)—a fall, however, which is quickly followed by a much greater rise in the antibody production, and corresponding with the latter there is an improvement in the clinical condition of the patient. In bad cases of boils or of furunculosis, however, it is necessary to give at least six injections at weekly intervals before the skin is cleared up: the result of this procedure, if successful, being a cumulation of the positive phase of antibody formation.

As a rule chronic cases are more suitable for treatment by ordinary vaccines than acute ones, but perhaps the best results are seen in some obstinate acute cases in which the temperature keeps up without any obvious reason. In vaccinating an acute case with an ordinary vaccine it is necessary to proceed with much caution owing to the serious effect of any diminution in the specific resistance of the patient. Among the acute cases that have been treated by vaccines are acute infections by the streptococcus, pneumococcus and B. coli—cases, that is, of cellulitis, erysipelas, puerperal sepsis, angina Ludovici, pneumonia, bronchopneumonia, colitis, etc. Among chronic cases treated by vaccine are prolonged suppuration of any kind, such as cystitis, colitis, empyema, and arthritis of gonococcal origin or due to some other suppurative focus such as pyorrhœa or a vaginal discharge. Some degree of success has also been obtained in a proportion of cases of persistent catarrh of the upper respiratory passages, and in cases of pruritus. Increase in the specific resistance effected by vaccination is often of only temporary duration, especially in those cases of long-standing localised infection where the general resistance of the patient has been undermined. It is important to bear in mind that the action of a vaccine is not to remove the cause of the patient's illness, but to stimulate his specific resistance to the fullest degree possible in the circumstances. Hence, in cases such as those of general septicæmia with meningitis, in bad cases of puerperal sepsis where the endometrium is found at the post-mortem to be sloughing, and in cases of ulcerative endocarditis, in all of which conditions the specific defence of the organism is already fully stimulated by the living bacteria at work in the patient's system, it is hardly a matter of surprise that the injection of ordinary vaccine is without effect.

Immune Serums.—If the object of giving a vaccine is to stimulate the patient to produce his own antibody, the second method of specific therapy supplies him with antibody already made by an animal such as the horse in response to vaccination. The best known of the immune sera is that which contains diphtheria antitoxin. The use of this serum has been one of the great successes of specific therapeutics. Potent though this specific remedy be, it is all important to give antitoxin early in the attack, and to give it in a large enough dose, *e. g.* at least 4000 units. Tetanus antitoxin has been much less successful. One reason for this is that by the time the patient develops symptoms of tetanus the specific conjunction of the toxin with his central nervous system has been already effected. Hence, in such cases the intraspinal or intracerebral injection of the serum is indicated. Another practical reason of the failure of tetanus antitoxin is the fact that these patients almost always have a mixed infection; the tetanus bacillus being associated with anærobic gas-forming bacilli, or B. coli, or streptococci, or perhaps with all three micro-organisms. Of the other immune sera the most notable perhaps is antimeningococcus serum. This is administered intraspinally in the following way. Lumbar puncture having been performed, 10 to 30 c.c. of the

cerebro-spinal fluid are withdrawn, and then, without removing the trocar, a similar amount of the immune serum is injected. The patient's head should be lowered after the injection in order to facilitate the circulation of the serum through his cerebro-spinal system. Of other serums antistreptococcus serum has proved useful in some acute cases.

In certain circumstances there is a source of danger in the use of immune serum from anaphylactic shock. This phenomenon of anaphylaxis is as follows—

If an animal is given a dose of the serum of another species—be that dose even a minute one—and an interval of from ten to twelve days or longer is allowed to elapse before another dose is administered, the animal on the second injection may undergo severe constitutional disturbance with collapse that may be fatal. If, however, the second dose of serum is given before the tenth day, there is no anaphylactic shock. Besredka, who has made a special study of the prevention of anaphylactic shock, or as it is termed "antianaphylaxis," has made the valuable discovery that anaphylactic shock is prevented if at the time of the second injection the susceptible animal is anæsthetised with ether, or if it is under the influence of a large dose of alcohol given either by mouth or by the rectum. Furthermore, he finds that if a small dose of the serum is given per rectum ten hours before, or subcutaneously five hours before, or intravenously five minutes before the second injection, it produces a condition of antianaphylaxis in an otherwise susceptible animal.

Sensitised Vaccines.—A third method of specific therapy which is now available consists of sensitised vaccines. This method was introduced by Besredka in 1902 and has certain advantages that deserve special mention. A sensitised vaccine is a vaccine which has been combined with the specific antibodies present in the serum of an animal immunised against the organism of which it is a suspension.

In making a sensitised vaccine all that is necessary is to leave the suspension of bacterial bodies in contact with immune serum at the room temperature for twelve hours. At the end of this time the bacteria of the vaccine have combined with their specific antibodies in the immune serum, and are agglutinated at the bottom of the tube. The supernatant serum is removed, and the deposit of bacteria is suspended in saline and then centrifugalised. The saline is removed, and the process of washing repeated. In this way all traces of serum can be removed, all chances of anaphylaxis obviated, and a vaccine obtained that is combined with its specific antibodies, or in other words is sensitised.

Besredka prefers to use living sensitised vaccines, but though this is probably the best method of immunising at present available, most people prefer to take no risk, and to kill the bacteria by adding 0·5 per cent. phenol to the saline with which the vaccine is washed after it has been sensitised.

During the ten years that have elapsed since the introduction of sensitised vaccines a large amount of experimental evidence has been accumulating with regard to their value, and it has been demonstrated that sensitisation of a vaccine has the following advantages—

1. The toxicity of the vaccine is enormously reduced.

2. The onset of the resulting immunity is accelerated.

3. It produces no negative phase or "reaction." It will be realised that these advantages make sensitised vaccines especially suitable for the treatment of acute cases, and they can be recommended for the treatment of acute infections by the Streptococcus pyogenes and by B. coli. Their clinical value in cases of pneumococcus infection is less established at present owing to the difficulty of getting an immune serum that thoroughly sensitises all strains of that organism. Similarly, in infections by the staphylococcus and by the gonococcus the difficulty is to get a serum that adequately sensitises a vaccine of these organisms. This difficulty, however, is unlikely to be a permanent one, and even a partially sensitised vaccine appears to have the conspicuous advantage over an unsensitised vaccine that it is less liable to produce a diminution of the patient's resistance.

Owing to the sensitisation it is possible to give sensitised vaccine in very much larger doses than the unsensitised.

In a series of cases of acute infection by Streptococcus pyogenes the writer obtained a marked improvement in a large proportion of the cases by giving doses 100, 500 and 1000 millions of the sensitised vaccine on three days in succession according to the intensive method of immunising devised by Fornet and Müller.

Such dosage and such a method of immunising would have been unsafe with ordinary vaccine. It was of interest to find that in two of these cases successfully treated with sensitised vaccine, ordinary vaccine and also antistreptococcus serum had been tried without avail. One of these cases, in fact, when the autogenous vaccine of streptococcus was pushed to 7 millions, developed a reaction with rigor and became distinctly worse; yet when this same patient was started with 25 millions of the same streptococcus after sensitisation, and the dose doubled every day for six days, he gave no reaction, but showed considerable improve-

ment; and after two more courses of sensitised vaccine he gradually recovered.

Sensitised vaccines would appear to be specially applicable for preventing infection in the case of epidemics, since they do not reduce the patient's resistance, and the resulting immunity has been shown by animal experiments to have already begun within twenty-four hours of injection.

They would also seem to have a field of usefulness in prophylaxis by raising the specific resistance of patients to sepsis before operation on the alimentary, urinogenital or respiratory tracts. Further they might be used medically in the same way in order to raise the resistance of patients to secondary infections which may be likely to occur at a later stage of their disease. M. H. G.

TREATMENT BY THE FINSEN LIGHT AND ULTRA-VIOLET RAYS

To Finsen, of Copenhagen, we owe the application of concentrated light to the treatment of diseases of the skin. The apparatus required is expensive, and the technique demands the constant attention of skilled assistants, factors which render its use in private practice impossible.

The essential features of the apparatus are—

1. A powerful source of light. In southern countries sunlight may possibly be used, but in Great Britain and in northern latitudes generally, a powerful electric arc is used. In the original apparatus of Finsen, an arc lamp giving a light equivalent to 30,000 candles is used, and this requires a special transformer or dynamo. The Finsen-Reyn modification can, however, be worked from the ordinary electric lighting mains (with a *continuous* current) and it gives equally good results.

2. A telescopic tube, provided with a series of rock-crystal lenses, by means of which the rays from the arc are first rendered parallel and then brought to a focus, this focus being the area under treatment. The telescope contains a column of distilled water, kept constantly cool by a water-jacket, to remove the heat rays given off by the electric arc.

3. A compressor applied to the skin at the focus of the rays. This compressor consists of a metal ring fitted with two plates of rock-crystal, the upper plate being parallel with the lower end of the telescope, while the lower plate, usually convex, is pressed firmly on the area under treatment. Through the compressor, a constant circulation of cold water is maintained to prevent the skin being burned by the concentrated rays emerging from the telescope.

The modus operandi is as follows—

The patient, suffering, we will suppose, from lupus of the face, is placed comfortably on a couch. The area to be treated, having been marked by a blue pencil, is brought exactly into the focus of the rays and then the compressor is applied with sufficient pressure to blanch the part. It is essential that the area under treatment be rendered anæmic, otherwise the actinic rays would not penetrate the skin. Having thus brought the spot to be treated in the focus of the rays, the patient is maintained in this position with the compressor held by a nurse (or in certain suitable cases fixed by a special apparatus) for one hour. The area treated is as large as a shilling. About six hours after the treatment the part becomes inflamed and a blister forms. It is essential that a blister should be produced; if vesication does not occur there has been some error in the technique, probably inadequate pressure, improper focussing, or dirty water in the telescope. The blister is dressed with a mild antiseptic ointment twice a day until healed. In cases of lupus this process is repeated until every part of the affected area is devoid of the nodules characteristic of the disease. Great care is taken to prevent irritation of the eyes. When the light has to be applied near them, the eyelids are closed and covered with layers of brown or red paper, which cut out the actinic radiations.

The condition in which this treatment excels is lupus vulgaris. It is especially indicated in lupus of the face, where the cosmetic result is of the highest importance. The scar is soft and supple, and, in many cases it is impossible, without the closest examination, to detect the site of the previous disease. The process is tedious, it is true, and demands considerable perseverance on the part of the patient and his attendant, but the results are worth the time and trouble expended to produce them. I have many patients, formerly entirely debarred from obtaining a livelihood by the disfigurement of their disease, who have been constantly employed at remunerative wages for years. As regards the permanence of the results, I have had many patients free from any sign of relapse for ten years.

A certain proportion of the patients are only partially benefited, and in these cases the disease has been widely spread, or there has been extensive disease of the nasal and buccal cavities. In a very small proportion the disease spreads too rapidly for the treatment to cope with its ravages.

When the lupus is of the ulcerative form, preliminary treatment of the pyogenic inflammation accompanying the tuberculous process is required, fomentation and the application of antiseptic ointments being necessary. In some

cases a preliminary treatment of ulcerative surfaces by X-rays has proved of great assistance.

Wherever necessary, the general condition of the patient receives the usual tonic treatment and extra nourishment.

Mercury Vapour Lamps.—A useful form of apparatus for producing a smart superficial inflammatory reaction by the actinic rays of light is the Mercury Vapour Quartz Lamp of Kromayer. This consists of a U-shaped quartz tube containing mercury vapour connected with an electric continuous current and enclosed in an envelope of metal, faced with a quartz plate. On the current being passed the tube is tilted so that the mercury flows from pole to pole and the vapour then becomes incandescent. The rays given off by the incandescent mercury vapour are intensely actinic. The heat rays are eliminated by a chamber between the source of light and the part to be treated, through which cold water is passed. An application of ten minutes is sufficient to cause a smart reaction with blistering, but the penetration is not so good as in the concentrated rays of Finsen's apparatus. Kromayer's lamp may be used for superficial forms of lupus. It is of more value in the treatment of some chronic forms of eczema, lichen, and in the flat warts of children.

Other Applications of Actinic Light.—Actinic light may be applied also to stimulate the growth of hair in certain forms of alopecia. Here I find Kromayer's apparatus is of service. A blue screen is used and the light applied for ten to twenty minutes to produce a definite inflammatory reaction. This need not go beyond an erythema, and can be repeated at intervals.

The treatment of vascular naevi by the Finsen light is very tedious, and other measures are preferable.

Lupus erythematosus of the chronic type occasionally reacts well to treatment by the actinic rays of light, but in practice I find that such cases are more amenable to carbon dioxide snow or to plasters, salicylic acid, etc.

J. H. S.

THE METHODS OF TREATMENT BY EXTREME COLD

The agents used in the treatment of cutaneous affections by extreme cold are: (1) liquid air, (2) solid carbon dioxide.

1. **Liquid Air** (temperature 182° C.) is procurable in special bottles made on the principle of the Thermos flask. The bottle is sent out in a box packed with straw to prevent jarring. Not less than one litre can be obtained, and this quantity generally costs fifteen shillings. It is, therefore, economical to have several cases to treat at one time, for the liquid air speedily disappears by evaporation.

To apply the liquid air sponge-holders holding lint or gauze swabs and a porcelain capsule are necessary. An assistant pours into the capsule the liquid air, which at once "boils." The swab held in the sponge-holder is dipped into the liquid and is immediately applied to the surface to be treated. I prefer to run over the whole area first rapidly and lightly, as this cools the surface and makes the following application more satisfactory. The swab is again dipped in the liquid and pressed firmly on the spot under treatment. This at once becomes white and looks as if a strong escharotic had been applied. The process is repeated until the whole area has been covered. In a few minutes, the white, hard-frozen patch thaws and resumes its normal appearance. When the face is being treated, care must be taken that the liquid air does not run into the ear or mouth, and the eyes must be carefully covered. Naturally, the eyelids must be avoided in cases of nævi.

After a varying time, from an hour to several hours, a blister forms containing clear serum. This is dressed as if it were a superficial burn, and the dressing may have to be continued for a week to a fortnight. It is exceptional to get any ulceration, unless the part has been scratched. In young children it may, therefore, be necessary to restrain the hands. When the parts are soundly healed, the treatment may be repeated.

The actual application is not very painful, but the thawing process causes intense pain, which, however, soon passes off.

2. **Solid Carbon Dioxide.**—The carbon dioxide or carbonic acid "snow" treatment was introduced by Pusey. It has the advantage of being much cheaper than liquid air, and the gas is easily obtained. When carbonic acid is released from a cylinder through a narrow nozzle into a bag, its escape causes a portion to be deposited as masses of thick flakes exactly resembling snow. The temperature of the solid is − 79° C. Gas cylinders containing seven to fourteen pounds are obtainable from the wholesale druggists.

A simple method of making the solid dioxide is to have a nozzle to fit the mouth of the cylinder, and to apply round it a washleather bag (a sponge-bag will do). The key of the cylinder is turned and the gas is allowed to rush out, at first in two or three short jets, and then for a longer period, according to the amount required. By touch, one is able to tell by the crackling sensation whether there is "snow" in the bag. The key is then turned off and the bag removed to a table or slab. Moulds made of metal or vulcanite of various sizes are now used to mould the snow into a solid stick. The

mould is provided with a rammer by which the snow is compressed. In treating a small area, care should be taken that the end of the stick is not larger than the spot to which it is to be applied. If necessary, the stick, which cuts like chalk, may be pared down or shaped with a penknife. In treating larger areas, square applicators are best, as it is easier to fit the squares together, or the method to be described presently may be used.

Various forms of apparatus for the making and moulding of the snow are on the market, and convenient portable cylinders with the necessary moulds can be obtained from the surgical instrument makers.

The stick or pencil of solid carbon dioxide, held in a piece of lint, is pressed firmly on the affected skin for from ten to forty seconds, or more, according to the effect required.

The result is a white, hard depression in the skin, which in five minutes fills up and resumes its normal colour. An inflammatory reaction with blistering, follows, and the inflamed, blistered surface is dressed with a simple antiseptic ointment. The treatment may be repeated when the reaction has passed.

There is comparatively little pain, except during the thawing process. If the application be too prolonged, especially if accompanied by strong pressure, sloughing may occur. Each application costs only a few pence.

Another method of applying carbon dioxide was introduced by Dr. W. K. Sibley. It consists in dissolving the snow prepared as above described in ether or acetone. The snow is dropped into a capsule containing the ether or acetone, and at once a "boiling" occurs. When a sufficiency of the snow has been dissolved, a jelly-like substance forms. This is applied to the affected surface on a camel hair brush, and the same whitening and shrinking of the skin occurs, followed by the return to the normal colour. This method is especially useful when treating areas of irregular surface or irregular outline, when it is difficult to get an even result with the solid stick. In using this solution, care must also be taken that the liquid does not run into the ear or the mouth. The after treatment is the same. In my experience, this method is attended by more pain than the application of the solid pencil.

Selection of Cases

Treatment by extreme cold is of value in some forms of vascular and pigmented nævi (moles), lupus erythematosus, superficial rodent ulcers, senile keratomata and warts. Success has been claimed in certain cases of lupus vulgaris, but the scope of the treatment in this form of skin disease is very limited. I have seen some very ugly scars on the face caused by prolonged endeavours to get rid of small patches of common lupus by the solid stick. At the bottom of the deep cicatricial pits characteristic nodules of lupus were plainly visible, although much healthy tissue had been destroyed.

It remains now to indicate briefly the special conditions in which the freezing treatment is indicated and some points of importance in dealing with them.

(*a*) **Vascular Nævi.**—The port-wine stain (simple angioma) can be treated by liquid air, and admirable results may be obtained if the nævus is not too deep. In all cases the surface becomes paler, but the treatment may have to be repeated again and again. Painting with carbon dioxide snow in ether is also suitable. The solid stick is not so useful, even when a square applicator is used, as it is almost impossible to get a smooth result, owing to the areas treated at each application being small and difficult to fit together; a mottled surface is a common result. I do not think that the results of either of these measures are so good as those obtained by radium, but the radium treatment of port-wine stains is a very tedious and costly business.

Nævus Cavernosus.—The raspberry mark of limited area, so commonly seen in infants, is best treated by the solid stick exactly moulded to fit the area. Moderate pressure is applied for about thirty seconds or more. The resulting scar is, as a rule, admirable. Care must be taken not to press too deeply or too long, or sloughing will occur, and this leaves an ugly scar. In the treatment of nævi of this variety on the face, I advise a first short application to avoid a disfiguring cicatrix. In many cases, one application is sufficient, but the treatment can be repeated after three or four weeks if necessary. If the snow pencil goes over the edge of the nævus, a white halo round the cicatrix is almost certain to be left and this makes the scar very conspicuous. Deep-seated cavernous nævi of the skin or subcutaneous tissue are best treated by electrolysis or by radium.

Stellate or *Spider Nævi*, the minute, rounded red spots with radiating vessels, common on the faces of children, are not suitable for the snow treatment. They are best dealt with by electrolysis or puncture with the fine-pointed cautery.

(*b*) **Pigmented Nævi** (pigmented moles).—Pigmented moles of small dimensions can be treated successfully by the carbon dioxide pencil, but the applications have usually to be repeated several times. A deep reaction is necessary because the nævus extends deeply. The hair follicles can be destroyed by this method if the subject be young. In older cases, electrolysis of the hairs may be required subsequently.

When the pigmented mole is of large dimensions, *e. g.* covering one half of the face or a large area of the body, the snow treatment is unsuitable. When the face is affected, the case should be referred to a surgeon skilled in skin grafting. The cosmetic result of such operations is not very satisfactory, and the child's parents must be allowed their option between an extensive mole, the nature of which every one knows, and a graft with its abnormal colour, which may excite even more comment than the birthmark.

(*c*) **Lupus Erythematosus.**—In the chronic variety of this disease, characterised by symmetrical, well-defined scaly patches on the cheeks, nose, etc., the application of the carbon dioxide pencil for ten to twenty seconds, or painting with the ethereal solution, often gives very satisfactory results. The reaction causes the formation of crusts, and, on their removal, a smooth cicatrix. Internal treatment by quinine, salicin, etc., must be carried on at the same time. Acute forms of lupus erythematosus should not be treated in this way. The result of such stimulation will very likely be an extension of the area of the disease.

(*d*) **Rodent Ulcer.**—Small superficial rodent ulcers can be removed by the application of the carbon dioxide pencil. I advise an application of at least forty seconds, with firm pressure. The reaction which results causes the parts treated to become inflamed and a crust forms, which should be allowed to separate spontaneously. A dressing of boric ointment may be applied. The application of the pencil may have to be repeated. The scar left is not so good as that following treatment by radium or curetting with subsequent application of the X-rays. I have several times been asked to treat by radium, or by curettage and the X-rays, cases of rodent ulcer which the snow treatment has failed to cure. In the deeper varieties of this disease, the carbon dioxide treatment is not suitable.

(*e*) **Senile Keratomata** are the flat yellowish-brown warty growths seen on the face and hands and elsewhere in elderly subjects. They may become malignant, and therefore require early treatment. They are, as a rule, readily removed by the solid stick applied as for the common wart.

(*f*) **Warts.**—The freezing treatment applied to common warts so frequently seen on the hands and fingers of children gives most satisfactory results. A pencil is shaped exactly to the size of the wart and is pressed firmly upon it for forty seconds. In large, hard warts, a minute's treatment may be given with advantage. The wart shrinks, but unless it is soft there is no depression left when the stick is removed. The wart soon resumes its original size and very often there is no inflammatory reaction, but the excrescence drops off in a few days, leaving a smooth, red surface. In some cases a second application is required.

The soft filiform warts of the scalp may also be removed by the application of the solid pencil. Occasionally, I have seen some septic inflammation follow from scratching the sores left by the reaction, and in one case this caused an acute inflammatory swelling of the warts treated, necessitating prolonged fomentation. The ultimate result, however, was perfect.

J. H. S.

RADIUM TREATMENT

The element Radium was discovered by Madame Curie in combination as a salt, but has since been separated in the pure state.

It is classified as a metal of the alkaline group and is very similar to barium. Its atomic weight is 226·5 times that of hydrogen; it is therefore one of the heaviest metals.

The bromide is the most active salt. It occurs in the form of small white crystals which are very soluble in water. It is hygroscopic, and if exposed to the air will gradually absorb sufficient moisture to become liquefied.

The chloride has the same properties, but is not as powerfully radio-active.

The sulphate and carbonate are white powders insoluble in water; they are also less radio-active than the bromide.

The term "radio-active" is now generally applied to a class of substances such as uranium, thorium, radium and their compounds, which possess the property of spontaneously emitting radiations capable of passing through plates of metal and other substances opaque to ordinary light.

The most remarkable property of the radio-active bodies is their power of radiating energy and heat spontaneously and continuously, at a constant rate, without, so far as is known, the action upon them of any external exciting cause. They also act on photographic plates and discharge electrified bodies.

The radiations from radium are very intense. The radium emanations are analogous to those of uranium and consist of three types of rays—

(*a*) Alpha (easily absorbed).
(*b*) Beta (penetrating).
(*c*) Gamma (very penetrating).

The *Alpha Rays* are readily stopped by a thin sheet of paper. They are used therapeutically in the form of the emanation either by inhalation alone or combined with oxygen, or by injection after absorption in water, oil or other media. A further field for their use is to deposit the emanation upon suitable substances and apply

direct to the tissues requiring treatment. Water takes up a very small percentage of the emanation; petroleum absorbs a much larger percentage, and it is possible that by this method we can obtain a highly charged substance which can be taken internally. The majority of the radium waters used therapeutically contain an infinitesimal quantity of radium; yet good results are claimed to have been obtained by using artificially prepared radium water, in gout, rheumatism, arthritis deformans, etc.

The *Beta Rays* are sometimes described as soft and hard; the latter can pass through several millimetres of lead.

The *Gamma Rays* are very penetrating and require several centimetres of lead to stop their passage.

The proportion of these rays given off from a quantity of radium is relatively—

Alpha	*Beta*	*Gamma*
80 per cent.	9 per cent.	1 per cent.

In practical therapeutics it is possible to utilise the radiations from radium by taking advantage of what is known of its physical properties. If, for instance, we desire to use the alpha radiation, we resort to one or other of the methods already described. For external applications on superficial areas the beta rays are more generally used. The radium is fixed upon a flat surface which can be made any size or shape, it is incorporated in a varnish and can be diluted to the required percentage by mixing it with a salt of barium. A thin sheet of gutta-percha tissue is used to prevent damage to the radium. The exposure is calculated according to the needs of the particular case undergoing treatment. Filters of aluminium can be placed between the radium and the tissue. The thickness of the filter determines the percentage of beta rays which are allowed to pass through. The gamma rays are stopped only by the thickest filters, and in superficial applications they also act; but the percentage present is so small that for practical purposes they may be neglected so long as the exposure given is a short one; in other words, during the exposure necessary to get a reaction from the beta rays, the gamma rays would exert no appreciable effect upon the tissues, whilst if an exposure be given of sufficient length to get an effect from gamma rays, the effect of the beta rays on the tissues would be destructive.

When it is necessary to obtain the gamma ray effect the filtration employed requires to be thorough; nearly all the beta rays must be cut off. This can for practical purposes be achieved by a filter of 2 mm. of platinum or 4 mm. of lead. In order to prevent the action of secondary radiations induced by the radium rays upon the platinum filter, it is necessary to inclose the platinum tube containing the radium in a rubber tube.

In the manner indicated it is possible to utilise all three or any one of the three radiations according to the method employed and the degree of filtration used.

Radium has during recent years had an extensive use in the treatment of many diseases, and results are published from time to time which enable us to assess its value as a therapeutical agent. It may be stated that it acts in a similar manner to X-rays in a number of diseases, and in our own experience in the majority of such cases the effect is the same: though at times it is observed that radium acts well when X-rays have failed to improve the condition and *vice-versa.*

It is therefore hardly necessary to refer *in extenso* to the many diseases where radium has been tried and found useful. The practical point to be noted is that in cases where the results obtained are equal, X-rays should be given the preference when the cost of radium treatment is so great. There are, however, diseases on which radium exercises a more beneficial influence, and these should be specially referred to.

Vascular naevi, especially in young children, come under this class. The results obtained may be no better than those from carbon dioxide snow, but the radium method is painless. The treatment takes a longer time.

Rodent ulcer, if treated early, readily yields to thorough radium dosage. The scars produced are good. Recurrence is apt to take place if the treatment is not carried on for a considerable time after the lesion has healed. Even after thorough prophylactic treatment, recurrences may be met with.

Lupus vulgaris frequently yields to radium treatment after other methods of treatment have failed.

Radium has been largely used in the treatment of skin diseases, and marked improvement may take place in very chronic cases. Amongst these are chronic eczema, psoriasis, lichen planus, pruritus.

Papillomata respond rapidly to radium.

Leucoplakia responds readily to radium treatment. In situations such as the mouth, tongue, etc., radium is probably the best treatment which can be employed, largely on account of the ease with which it can be applied to the leucoplakia patch. This condition is frequently a forerunner or an accompaniment of cancer. When the latter disease has established itself, it renders the prognosis more grave, though very early cancer may be healed for a time at least. Prolonged treatment is necessary, and the radium applicator has to be well screened to avoid damage to the healthy tissues.

Radium in the Treatment of Malignant Disease

It is here that radium has found such a large field for its therapeutic properties. When first used in treatment, great hopes were entertained that at last we had an agent which would exercise a beneficial effect upon malignant disease and particularly upon cases of cancer. Enthusiasts in radium therapy spoke of the selective action of radium upon the cancer cell. That radium does exercise an influence over a morbid process in tissues no one will deny; but that it possesses a selective action on cancer cells only even its most enthusiastic supporter will now hardly affirm.

Many cases of all varieties of malignant disease have been treated with radium, some with benefit, others with none. Numbers may have been influenced in the wrong direction. We are still in the dark as to its exact action on these growths, nor can we foretell which particular case is likely to respond favourably to treatment.

Sarcoma, the round-celled variety, frequently responds well to radium. Such tumours may disappear after careful treatment, which should be continued for a considerable time to, if possible, prevent recurrence. Recurrence after operation has been successfully treated by long exposure to well-filtered radium dosage.

Lymphadenoma and *Lympho-Sarcoma* also respond to radium; but relapses are common with this as with other forms of radiotherapy.

Endothelioma is particularly amenable to radium treatment. When situated in the mouth or pharynx, radium is practically the only non-operative method of treatment we possess. The same applies to epithelioma and other forms of cancer. The tubes containing radium may be fixed in position and left for the necessary time.

Superficial Epitheliomata of the skin respond well to radium treatment, but there is the great drawback (which should always be kept in mind) that one can never tell when a particular case is likely to do well. Valuable time may therefore be lost if cases are treated with radium only. A good method is to excise the growth and treat afterwards with radium in the hope that recurrence may be prevented.

Cancer of the œsophagus may be treated by passing a radium tube into the stricture; the tube is kept in position by means of a length of silver wire which can be carried out at the mouth and fixed outside. Unless the radium tube can be passed directly into the stricture it is unwise to attempt to treat a case, because the healthy mucous membrane does not stand such long exposure as the growth, and serious damage may be the result of the treatment.

Cancer of the cervix uteri. When the disease is too extensive for operation to hold out any hope of relief, the condition of the patient may be greatly relieved by radium treatment. A preliminary curetting of as much of the growth as possible is helpful, the radium can then be carefully packed in position and the necessary exposure given. It is noteworthy that a marked diminution of the growth can be brought about by repeated treatment at regular intervals. Hæmorrhage may be checked, and discharge lessened. Several cases have shown marked improvement.

Cancer of the body of the uterus may be relieved by inserting radium tubes into its cavity. Recurrence of the growth after operation has occasionally to be treated, and the condition of the patient is frequently rendered more tolerable by radium treatment.

Cancer of the rectum may be treated by passing tubes into the stricture. Here, again, emphasis should be laid on the point that it is absolutely essential that the tubes should be placed in the midst of the growth. This can only be done when the lumen of the bowel is still patent and the growth involves the whole of the bowel. The growth shrinks and the function of the bowel may be restored for a time if a sufficient quantity of radium is used and a long enough exposure is given.

Recurrent cancer of the breast is treated by radium sometimes with a definite measure of success. In the majority of cases, however, X-rays do as much for the patient.

Inoperable cancer of the breast may be treated by several methods—

(1) External application of a number of tubes covering the whole area in sections giving an equal exposure to each.

(2) By inserting the tubes directly into the substance of the growth.

(3) By combined X-rays and radium treatment.

The writer has employed all three methods. Buried radium tubes have exercised a marked degree of action, but no individual case has resulted in cure.

One case treated by X-rays and radium cleared up and the patient remains well.

The degree of success attending the radium treatment of cancer is dependent on so many factors that it is at present impossible to make any definite statement on the point of its actual value. We can, however, state that slowly growing cancer which possesses a large percentage of fibrous tissue in its substance is more readily influenced than the rapidly growing cellular type. Some writers claim that the latter type readily responds to treatment. Rapidly growing cancer in young patients is hardly ever influenced by radium treatment.

The legitimate use of radium in the treatment

of cancer in the present state of our knowledge should be confined to—

1. Prophylactic treatment before and after operation. A few exposures can be given while the patient is waiting for operation. Tubes may at the operation be left in the wound and withdrawn after the necessary exposure. When the wound has healed, exposures should be given at intervals of about five weeks for a considerable time afterwards. Prophylactic treatment by X-rays appears to be as efficacious and is certainly more easily applied.

2. Cases of growth where the patient refuses operation should be treated thoroughly for a long period. It is in this group of cases that good results are occasionally met with.

3. Inoperable cases of cancer may by radium treatment be reduced to a state where operation is possible.

During the treatment of particular cases by radium the writer has been greatly impressed by the manner in which large masses of growth or large malignant ulcers have quickly disappeared, ultimately leaving a sound scar in place of the mass of growth. This seems to indicate that radium possesses a marked influence over the growth of these morbid processes. To a certain extent this is true, but in the adjoining skin which had been exposed to the radiations, new growth has appeared. A radium tube inserted into the newer growth quickly caused it in its turn to disappear. Later, however, large masses appeared at more distant parts. Observations of this kind raise the question of metastases—Did the radium stimulate the growth to such a degree of activity that its spread to distant parts was accelerated?

The local treatment of a growth does not appear to prevent its spreading in a number of cases. This may be due to the incomplete destruction of the cells of the growth. Further, it is just possible that unless the action of radium is very rapid and quickly kills all the cells, they may assume a marked degree of activity.

Observations of this kind suggest that in all cases of cancer suitable for operation the latter method should be employed and prophylactic treatment vigorously carried out afterwards, rather than run any risk of delay by experimental treatment by radium. The same routine treatment of malignant disease should be employed when using X-rays or radium. The most important point is to get the effect quickly, next, to prevent recurrence in the immediate vicinity of the local disease, the whole area of lymphatic distribution around the central area should be well irradiated in the hope that the tissues will resist further invasion. In some instances, if the exposure is too long or the filtration insufficient, a necrosis of the growth and the surrounding tissues results, all the tissues participating in the changes to a varying extent according to the power of resistance of the particular elements of the growth and the adjoining tissues. Thus, blood vessels become occluded, muscle fibres undergo a fibroid change and atrophy, nerve bundles become inflamed and later degenerate, mucous membranes slough, gland tissue becomes necrotic and the skin undergoes changes according to the intensity of the irradiation.

It has been observed on several occasions when patients have been subjected to long and repeated exposures that an extremely painful condition is set up in the neighbourhood of the tissues treated. This is particularly evident when the lesion is situated near the large nerve plexuses. It is probably due to neuritis and perineuritis of these large nerves and is troublesome and difficult to relieve.

In cancer of the breast treated by buried tubes in the substance of the growth, where the tumour has not yielded to radium treatment, or only partially so and a considerable degree of necrosis of breast tissue has followed with a degree of fibroid change, an intolerable amount of pain has followed. In one case the only remedy that could be suggested was the complete removal of the breast, and the severing of as many nerves as possible in the vicinity of the growth.

It should be always borne in mind in all cases treated by radium, where a considerable reduction in the size of a tumour has resulted, that, when it has been reduced to an operable condition, time may be saved and extension of the disease prevented if the radium treatment is combined with operative measures and prophylactic treatment is continued after the operation. R. K.

REST-CURES

The easiest thing in the world is to prescribe an orthodox rest-cure. It gives the physician rest as well as the patient. It saves all the worry and trouble of investigating fully an obscure case, and does away with the difficulties of individual treatment. In his well-known work on *Fat and Blood*, Dr. Weir Mitchell, referring to the form of treatment known by his name, says: "I am more fearful that it will be misused, or used where it is not needed, than that it will not be used, and, with this word of caution I leave it to the judgment of time and of my professional brethren." His prophecy was correct. The Weir-Mitchell rest-cure has become a stereotyped prescription, a conventional remedy that patients will even demand of their doctors themselves. We propose to describe very briefly the orthodox rest-cure, to analyse the curative elements that

it contains, and finally to discuss the types of cases requiring various forms of rest-cure. Weir Mitchell devised the rest-cure as a combination of psychic and physical influences, suited to the requirements of a fairly common type of neuropath. It comprises rest in bed, isolation, superalimentation, and massage. The typical routine is as follows—

7 a.m. Cocoa; cool sponge bath; rough rub.
8. Breakfast (ordinary full meal) with milk; an hour's rest.
10. 8 oz. peptonised milk.
11. Massage.
12. 8 oz. milk or soup; nurse reads aloud ½ hour.
1.30. Dinner (ordinary diet, two-course); 1 hour's rest.
3.30. 8 oz. peptonised milk.
4. Electricity; rest until—
6.30. Supper (ordinary diet, milk); rest.
8. Reading aloud ½ hour.
9. Light rubbing.

Weir Mitchell considered massage to be of the greatest importance in taking the place of exercise and counteracting the evils of prolonged rest, and on this account he preferred a bad rubber to no rubber at all. On the other hand, electricity was considered the least essential item in the prescription. A programme of this kind is calculated to act in a threefold way, on the emotions, the intellect, and the organism. The emotions are influenced by the isolation, it may be, from unwise sympathy or domestic friction. The intellect is influenced by inactivity, because no effort of any kind is permitted, and the body is affected by rest in the horizontal position, by diet and by massage. Now it is obvious that without more insight into the nature of our cases we cannot hope to determine successfully the exact therapeutic indications for each. There are some special characteristics of the neuroses to be considered which may serve as keys to treatment. The first thing is to decide whether the symptoms are purely defensive. Defensive symptoms have as their object the removal of the patient from an intolerable situation. The intolerable situation may exist in the material environment or may be due to the entry into the mind of ideas that are incompatible with the patient's personality. A man who finds his work uncongenial, or fears some element in it, may begin to exaggerate unconsciously some simple organic symptom until it becomes a successful defence against continuing that work. He passes from a transitory and accidental state of health into the organised neurosis. In the second eventuality the handling of the mental situation gives a greater range of results and reveals its final products in an infinite variety of ways of which the commoner are the obsessions, the phobias and the hysterical accidents. It must be borne in mind that it is useless to regard defence symptoms as due to fully conscious and wilful motives. Such an attitude only can lead to disaster. It is obvious that if a patient develops a defence symptom against an intolerable situation in the world, and is advised to take a rest-cure that three things at least may happen—

1. He may recover during the cure and relapse instantly when placed once more in the old situation.
2. He may be dominated by the idea that so soon as he recovers he will have to go back to the intolerable situation, and remain uninfluenced.
3. He may see things in a new light or find a solution to the problem during the cure, in which case he will speedily get well.

If a patient is suffering from a defence symptom that has arisen through moral conflict, and has freed himself from that conflict by the development of an obsession or other psychoneurotic manifestation, it is obvious that a pure and simple rest-cure is not likely to assist him. It may, and usually does, increase his distress.

From the above considerations alone it will be seen that it is important to gain some idea of the psychology of the patient before one can honestly prescribe a rest-cure. Since the state of mind is not apparent after testing the reflexes or examining the fundi, it is necessary to go into the patient's life history as fully as possible and urge investigation precisely in the direction of those matters which he seems least inclined to discuss. For this purpose it is a great mistake to force the patient to sit in a strong light. It is difficult for any one to talk of those factors that are powerful enough to produce defence symptoms and doubly so, if seated in the glaring light that convention usually associates with a medical examination.

The second factor to be considered is the amount of pain endured by the patient. Severe pain demands rest whether it be defensive in a psychological sense or defensive in the physiological sense of Hilton. But to Hilton's clinical conception of the importance of rest in pain must be added the view that pain may persist apart from material causes, and remain uninfluenced by bodily quiescence. Here one is apparently dealing with something that differs from inflammation. Pain may be persistent in a limb without any demonstrable modification of tissue. In such a case it will be unprofitable to direct treatment solely to

the prominent symptom, by the injunction of rest, and pay no attention to hidden factors. Mental tension, induced by worry, will express itself in many patients, particularly neurasthenics, in the somatic sphere by an aggravation of pain.

The third factor is that of nutrition. A condition of emaciation with its accompanying physical weakness is the most decisive signal for rest.

It is possible to summarise the above factors under two headings. Every patient presenting himself for examination must be considered from two standpoints, and his symptoms classified under two headings—

1. **Physiological Defence.**—By this is meant the normal reaction of the body to strain and exhaustion.

2. **Psychical Defence.**—By this is meant the special reaction of the patient's mind to his environment, and its expression in bodily and mental symptoms. The more fully (1) is represented, the more successful will the ordinary rest-cure prove. When (2) is chiefly present, the ordinary rest-cure will give very poor results. A person who breaks down through sheer pressure of work will present factor (1) most emphatically, and will derive benefit from rest. A person who breaks down owing to a tragic love affair will present factor (2) most prominently and will perhaps only be made worse by rest.

It will be seen, therefore, that for a large number of cases something more than simple rest, superalimentation and massage is required. Treatment can be directed, roughly speaking, in two ways. We may aim at increasing the patient's powers of resistance by discipline, re-education of attentive control, by suggestion, and persuasion. In this way we add something to the patient, and take nothing away. Or we may endeavour by a process of analysis to remove some of the patient's difficulties, and make clear to him how and why his troubles have arisen. By this method we take something away from the patient so that with his customary powers of will he is in a better position to handle the problems of his life. The comparatively small amount of insight that an average person has into the causes of his own behaviour or into the factors that produce a recurring and typical experience in his life makes psycho-analysis of great value. The aim of the analyst is not simply to tell the patient the nature of his difficulties, but to make him realise them for himself. The function of the analyst is to hold the mirror.

The emotional factor in the rest-cure requires special consideration. In neurasthenia the patient must be isolated from all sources of worry, strain, anxiety, perplexity and excitement. He generally needs a judicious amount of sympathy—indeed, many cases of neurasthenia, especially in young girls, are largely caused by lack of sympathy in the home or chronic conflict arising out of emotional antagonisms. The doctor tells her that she must "pull herself together," the mother has suggested that she should not think so much of herself, and the father has hinted that it is "all rubbish and hysteria."

In hysteria, on the other hand, the primary indication is isolation from sympathy. The hysteric must be removed from the possibility of causing excitement or commotion. She must be in an environment where hunger strikes cause no consternation and where broken windows arouse no amazement. In other words she must be removed from her audience and learn to appreciate the pleasure of a normal objective existence as opposed to her previous life of melodrama. But in this there is need for a word of caution. The genuine hysteric is convinced of her inability "to pull herself together." If she is treated with too direct discipline or scepticism, she will pose as the misunderstood martyr, and once this attitude of self-pose has been fairly established, we are very near the borderland of dual personality. Clifford Allbutt goes so far as to say that the Weir-Mitchell rest-cure is of no specific value in hysteria, except in so far as any removal from home and submission to medical discipline is effectual. The question of discipline is all-important. There must necessarily be a great deal that is distasteful to the hysteric in the monotonous seclusion of the rest-cure; and it is, therefore, of paramount importance that the doctor should feel that he has the necessary support and confidence of the relatives to enforce his authority. If the patient begins the cure "just to see what it is like" or if she feels that a pathetic appeal, or an insistent complaint would suffice to persuade her people to take her home, then the cure will be limited in its results. If it is necessary to humour the hysteric in order to keep her under treatment little can be achieved except in mild cases. There is no royal and pleasant road to develop inhibition. The doctor who shirks responsibility in this respect is simply neglecting a sacred duty, although he may be pleasing the patient.

On the other hand, the neurasthenic should, and will, enjoy a rest cure, provided it is conducted on rational lines. If she is a true neurasthenic and yet finds the cure irksome there must be something wrong with the cure. In the original Weir-Mitchell treatment what was chiefly wrong, from the point of view of the true neurasthenic, was the amount of time given to so-called rest, with no form of distraction.

The result was worry and increased introspection. This brings us to consider the intellectual aspects of the rest-cure. There are three lines of treatment in this respect—

1. Mental inactivity.
2. Mental occupation without effort.
3. Mental occupation with effort.

The Weir-Mitchell cure provides a great deal of the first, very little of the second, and none of the third, and it is in this respect that there is the greatest scope for adjusting the cure to suit the individual needs of the patient. We should ask ourselves how far the patient is capable of concentrating his attention, how far this degree of concentrative control is less than his normal power, how far the condition is due to undeveloped or deficient thought control, and how far due to overtaxed and abused concentration. The typical hysteric has little power of concentration unless in extraordinary circumstances. Volitional attention is of the weakest order. She lives in a chronic state of diffuse and spontaneous attention, with the threshold of consciousness abnormally low. Her power of determining her own area of consciousness is inadequate. This being so, re-education of the attention is essential, and the patient must be drilled in every form of exercise that will contribute to this end. The neurasthenic, for the most part, is unable to concentrate from sheer fatigue, and according to the stage of the complaint the indication is for absolute passivity, or for distraction without effort. Clifford Allbutt says: "In hysteria the key to successful treatment is active impulsion; in neurasthenia it is rest, rest, rest, in all directions but under such conditions as to avoid a cloying or rusty sluggishness."

Finally, we come to the physical aspects of the rest-cure. The first of these is rest in the horizontal position. In many cases this is clearly indicated, but there are cases in which the most perfect rest cure does not imply confinement in bed. Apart from neuropathic indications for prolonged rest in bed, we have to bear in mind such physical factors, incidental or concomitant, as circulatory insufficiency, gastroptosis, and floating kidney. In Weir Mitchell's original scheme superalimentation occupied almost the first place of importance. His views about fattening and blood-forming have for their foundation his abhorrence of drugs in any shape or form. One is often inclined to question the wisdom of this ruthless overloading of the stomach when some preparation of malt would go a long way towards fattening the patient, while injections of iron, with or without arsenic, would make up any deficiency in red blood-corpuscles or hæmoglobin. This is an item which should be adjusted to individual requirements and not blindly accepted as an integral part of all rest-cures. The question of massage, electricity and exercises must next be considered. Taking the cure as a whole, massage is imperative. Prolonged rest coupled with over-feeding would spell failure without it. But if the cure is modified massage may be wholly uncalled for. For the hysterical, it is best to avoid massage. She is apt to like it too much. Swedish and Müller's exercises answer better. As a rule we prefer electrical vibratory massage to manual massage. The value of electricity in neuropathic cases is chiefly suggestive, as most prominent electrotherapists admit. Static electricity seems to us to give the most satisfactory results but the indications are always empirical, and suggestion by itself, without cumbersome apparatus, is a simpler method of procedure. Exercises are of great value. They must be graduated, from mere Nauheim exercises to the most violent digging, and from croquet to club-swinging. The psychic element must be remembered in all work and exercise. Manual labour may be physically indicated, but it may be too monotonous to prevent introspection; walking may be indicated or otherwise, according to the companion available; motoring may be the cure of the man who drives himself, and harmful to the patient who is driven; dumb-bells may be used mechanically, but Indian clubs cannot.

For mental occupation card games are a great resource; Patience is almost invariably useful, and the ideal nurse should be able to teach the patient the varieties of this game. No burden must be laid on the memory of the neurasthenic. The contrivances known as jig-saw puzzles are valuable. Patients should be encouraged to do things in accordance with a self-imposed time-table, and be independent of their feelings of fitness or otherwise. The time-table should be made out every evening for the following day. This increases self-confidence.

As regards the nurse, the greatest mistake she can make is to fall into the error of professionalism. The solemn and sacred rite of taking pulse and temperature with an air of mystery is a sweet morsel to many a hysteric, in whom the doctor is trying to inculcate some degree of healthy-mindedness.

We have surveyed as briefly as possible the general aspects of rest-cures. The particular methods of treatment applicable as adjuncts during the cure are discussed in other articles. Both in suggestion and psycho-analysis we have two powerful weapons with which to combat the graver cases of neuropathic disorder. In conclusion we mention a few points of success and failure. If an hysterical patient is treated as a neurasthenic, the results will be transitory.

If a neurasthenic is treated as a hysteric, there will probably be no results at all. If a case of neurasthenia due to eye-strain goes through the orthodox cure, he will improve rapidly at first, slowly towards the end, and relapse instantly when he resumes work. Many rest-cures are begun, endured and paid for, that might have been avoided by seeking the advice of a competent oculist. All cases of toxic neurasthenia tend to improve chiefly on account of the massage, but there is little to boast about if one cures for the moment a patient who should have had a vaccine for some hidden suppurative process. Finally, the aim of every rest cure should be not only to put the patient on his feet again, but to teach him never again to fall; and to do this two things are essential—the avoidance of routine and the most careful and painstaking study of the psychology of each case.

H. C. M.
M. N.

TREATMENT OF THE SPECIFIC INFECTIOUS DISEASES

THE GENERAL TREATMENT OF INFECTIOUS FEVERS

The fevers included in this section are **Chickenpox, Diphtheria, Measles, Mumps, Rubella, Scarlet Fever, Smallpox, Typhoid Fever, Typhus** and **Whooping Cough.** Cerebro-spinal Fever only receives notice in regard to prevention, as its clinical aspect is dealt with elsewhere. Being a very doubtful entity, the "Fourth Disease" is not mentioned. Repetition throughout the section is avoided by treating common points collectively and noting special ones as they arise. So considered, the subject falls naturally under eight heads: beginning with (1) prevention, the others are the treatment of the infective process by (2) specific means or (3) chemical germicides; (4) of local lesions, mainly by antiseptic applications; (5) of the febrile disturbance; (6) of related factors in this disturbance; (7) of cardiac weakness by direct measures; and (8) of the post-febrile state.

I. Prevention

1. The Control of other than Clinical Sources of Infection.—Such sources, the habitats of pathogenic germs, are, with possible rare exceptions in certain fevers, either carriers or contacts liable to develop an infection. Temporary carriers of the diphtheria bacillus, the meningococcus, or the typhoid bacillus, may be isolated in special circumstances, but the rule is to warn all carriers as to the modes of direct or indirect contact which may be dangerous to susceptibles, and to employ local antiseptics for what they are worth when the organism concerned is the diphtheria bacillus or the meningococcus. Contacts kept under observation over the quarantine period of a fever need seldom be isolated. In *Diphtheria*, with some uncertainty of result, antitoxin prevents the development of an attack and is used for children, but for adults it has the disadvantage that serum sickness may keep them from work for a week or even longer. When a case of *Smallpox* occurs, any unvaccinated infant or person in the house should at once be vaccinated, and all adults and younger persons over the age of eight revaccinated. For about three days after exposure, vaccination will usually avert the coming attack if infection has taken place. In practice, all contacts are vaccinated so long as symptoms of an attack are absent. Strict isolation and disinfection are ordinarily reserved for actual cases of the various fevers.

2. Isolation in Hospital.—*Smallpox* is removed to a special institution on a secluded site. Regularly or incidentally admitted to fever hospitals, the other diseases are for the most part segregated with their kind in large wards and there nursed in common. However, by complete or partial separation with asepsis, or by means of the latter alone, it has been found possible to utilise the same nursing staff for diverse infections. Such methods of unit nursing include the barrier system, bed isolation, and the use of cubicles, corridor cells, veranda cells, and open-air shelters. Tests with some fevers have not passed the experimental stage, but the available evidence is to the effect that when the beds are at a sufficient distance from each other, asepsis alone will control all those in view, except *Scarlet Fever, Measles* and *Chickenpox*, if fresh air is supplied freely. The non-convection of the last three by the air of well-ventilated wards, and the possibility of safeguarding susceptibles from their virus when carried by other vehicles at close range, must remain an open question until the observations of Rundle and Burton at Fazakerly Hospital are tested further or proof is obtained by some other method of investigation.

3. Isolation at Home.—The quarters chosen, including a room for the nurse, and, if possible, a bathroom and w.c., should be at the top of

the house or in a passage which can be closed to the family. They should be stripped of furnishings to the hospital standard and barriered off from the rest of the house by a suspended sheet kept moist with 1 in 60 carbolic lotion.

4. **Disinfection.**—Subject to supervision by the medical man, this, of course, is entirely in the hands of the nurse. She works in four zones—

(A) *At the source.*—The points at which discharges leave the body are in most instances determined by the location of inflammatory tracts, and it is the rule to treat all such discharges as infective. With exclusive isolation, however, their control in *Smallpox* at this stage is more a matter of cleanliness than prevention. (*a*) The *nose* and discharge from it are chiefly treated in *Cerebro-spinal Fever*, nasal *Diphtheria*, *Measles*, *Scarlet Fever* with rhinitis and *Whooping Cough*. The nasal cavities may be sprayed from time to time with an antiseptic while gross discharge is frequently swabbed away from the nostrils. (*b*) Discharge from the *mouth* may be due to stomatitis, or to the sore throat of *Scarlet Fever*, *Diphtheria*, etc. A syringe clears out the mouth and throat most effectively. If there is a trickle from the mouth, it is removed by swabbing. Sputum, as in *Whooping Cough*, is collected in a spit-cup containing 1 in 20 carbolic lotion or on a piece of rag, afterwards burnt. (*c*) The *ear*, in the otitis of *Scarlet Fever*, *Diphtheria*, etc., is syringed out and at other times covered with absorbent wool. (*d*) The *eye*, when discharging in *Smallpox*, etc., is washed with a mild antiseptic and, if necessary, an absorbent dressing applied without pressure. (*e*) The *skin*. Milne maintains that *Scarlet Fever* will not spread under any conditions of contact if, from the outset of an attack, firstly, the tonsils and pharynx are swabbed with carbolic oil (1 in 10) every two hours for twenty-four hours, and, secondly, pure eucalyptus oil is rubbed over the entire skin every morning and evening for five days and then once a day until the tenth day. The method has failed at Plaistow Hospital, where early treatment is seldom possible, but in view of the evidence adduced in its favour, the writer considers it well worth a trial in private practice. *Measles* has been similarly treated. Secondary cutaneous sores, most frequently caused in *Scarlet Fever* and *Diphtheria* by irritating discharge, are covered with a dressing, unless their position on the face makes this impossible, when they are thickly smeared with lanoline or some ointment. As infective sources, their prevention is important. (*f*) The *anus and urethra*. It is only in *Typhoid Fever* that the disinfection of excreta is attempted in this country. The standard proprietary germicides which emulsify with water are more reliable than carbolic acid for this purpose. Half-an-ounce, with about twenty times as much water, may be put in the bed-pan. Two drachms, undiluted, are added to ten ounces of urine: more or less in proportion. If crude carbolic acid is employed, the quantities are the same; it is placed, pure, in the bed-pan or urine bottle when the utensil is taken from the bedside. All germicides are stirred through the fæces or urine with a piece of stick, which is then burnt. An hour is supposed to be allowed for their action before the utensils are emptied, but in practice the nurse is commonly compelled to dispense with this precaution. Moreover, disinfection at best remains uncertain, and the destination of the excreta is thus more important. In a sewered district there is no objection to discharging excreta into a w.c., and this course is usually taken. Burial, again, may be the only available resource in the country. Where there are no sewers, the disposal of evacuations during an epidemic is a question for the Local Authority; they may be collected and buried or burnt. Urotropin as a vesical disinfectant is mentioned in Part II. (*g*) Inflammatory discharge from the *vagina* is rare, but least so in children who have *Scarlet Fever*. It is controlled by disinfection and an absorbent pad.

(B) *On the bed.*—For all the careful collection of visible discharges and the use of check splints to keep children from dabbling in those coming from the mouth, nose, eyes and ears, a portion is certain to escape and reach the bed, which is also exposed to particulate impregnation. Thus the bed becomes, as it were, a trap for the contagium which passes the first zone, and is placed about eighteen inches from the wall to prevent the patient from touching the latter. When discharge comes from the mouth or nose, or there are uncovered sores about the face, gross soiling of the pillow is guarded against by using an inner case of jaconette or batiste. Fever patients who have discharges should wear a linen or cotton nightdress rather than a woollen one; a vest of wool will serve as additional clothing and can be sleeved if needful. The mattress, in the case of young children and older incontinent patients, is protected by a mackintosh under the sheet. Over the latter a drawsheet, folded to form a broad strip, crosses the bed with its centre under the buttocks. A hospital drawsheet is single; for *Typhoid Fever* with diarrhœa, it has a narrower mackintosh under it. A sheet is always placed next to a patient who passes excreta in bed, as it partially saves the overlying blanket from contamination, and the

nightdress is slit all the way up the back. Taking these coverings as a whole, their object is not only to facilitate the collection of discharges, but to make changes less tiring for the patient and easier for the nurse, and to give less work in disinfecting and washing.

(C) *On or in vehicles away from the bed.*—*Cerebro-spinal Fever* and *Rubella* are not known with certainty to infect indirectly, and the other acute infections, with the exception of *Typhoid Fever*, are more often contracted during close association with patients than carried deviously by vehicles. Nevertheless, all contaminated articles are disinfected. (*a*) The nurse's hands have constantly to be cleansed in the course of her work, and she has to protect her uniform from gross soiling, if need be, by wearing an overall. (*b*) Some crude carbolic acid or other disinfectant is added to waste syringing and douching solutions not in themselves definitely germicidal. Water which has been used for washing and bathing is similarly treated, especially if the disease be *Typhoid Fever*. (*c*) Dressings, swabs, etc., are burnt, with such used food and rubbish as are combustible. (*d*) Stains caused by discharges and excreta are washed out of cotton, linen and woollen articles, including blankets, by pouring water through the soiled part into a bucket, w.c., or, in hospital, a hopper. Linen and cotton articles, with others of the same kind not visibly soiled, are steeped in an emulsifying disinfectant (1 in 40), well rinsed in pure water, and boiled at the time of washing. Woollen clothing and blankets, after stains are removed, have only the cleansed parts exposed to the disinfectant by laying them over a bucket containing it. They are not steeped as a whole or boiled. (*e*) Suitable articles (medical, surgical, nursing) are sterilised by boiling. (*f*) As water carries the contagium of *Typhoid Fever*, that required for the household may have to be boiled, especially if the local supply or public service is under suspicion. (*g*) *Diphtheria*, *Scarlet Fever* and *Typhoid Fever* are spread by contaminated milk. Hence, when the source is doubted, it is boiled, and in any case the supply for a family should be separately stored from that used for a patient. Hospital nurses should not be allowed to take food, milk, beverages or water, while on a division used for cases of Typhoid Fever. If they become infected, it is generally found that this rule is not enforced or has been broken. (*h*) Flies are difficult to control, and as they are attracted by discharges both at the source and as carried by vehicles, seek out food, and may settle on the face of susceptibles, it is reasonable to believe that they transmit infections. Fly-papers and fly-traps are almost useless unless open windows are screened with gauze and doors kept closed. Flies may be kept off patients who have discharges or sores in the region of the face and head by attaching one edge of a gauze square half-way up the head-rails and fixing the opposite side to the chest. If the infection is one borne by milk (par. *g*), vessels containing it should be covered. In *Typhoid Fever*, all stored food should be so protected, bed-pans and urine bottles covered until they can be cleansed, and the exposure of stained linen, etc., avoided. The prompt burial of excreta in country practice is also indicated; typhoid bacilli have been found in flies. (*i*) Air may be a vehicle of *Diphtheria* and doubtless also of *Measles*, *Whooping Cough*, *Scarlet Fever*, *Cerebro-spinal Fever* and other diseases, when patients or carriers cough, sneeze or speak (droplet infection). Medical men and nurses have to be careful in this respect when close to patients. As regards what may be termed atomic dispersal of virus, the existence of which it seems necessary to accept, free ventilation is apparently an all-round safeguard, though more effective in some diseases than others. It is largely relied on to protect medical men and nurses from *Typhus*, now commonly treated in the open air. (*j*) Transference by third persons, other than medical men, nurses and carriers, is prevented by strict isolation, but in actual fact normal contacts are infrequent vehicles, except possibly in the case of *Smallpox*.

(D) *At large in the sickroom or ward.*—It has still to be proved that infection due to germ-laden dust, if it does occur when a fever has a relatively resistant virus, is common. Meanwhile all dust is treated as infective. At one end of transference, the nurse is expected to remove fouled articles before gross discharge can dry. At the other, she should, before sweeping a ward, scatter some damp substance on the floor; in a private house, cover her broom with a cloth wrung out of 1 in 20 carbolic lotion and use a duster similarly damped.

5. **Periods of Detention.**—In *Cerebro-spinal Fever*, the meningococcus is rarely present in the naso-pharynx when two months have passed from the commencement of an attack, and has usually disappeared long before this period, but as more persistent convalescent carriers exist, a bacteriological examination should be made before patients are released, and conditions laid down if the germ is found. Cases of *Chickenpox* are free from infection when all scales and scabs have come away. Persistent lesions which have lost their first crust are very rarely infective. Those recovering from *Diphtheria* are held to be possibly infective so long as the discharge and sores due to it persist, unless the bacillus is shown to be absent from these lesions, and until three successive cultures from the nose and throat

prove negative. However, even in the absence of the culture-test, return cases are extremely rare in hospital practice. Three weeks' isolation is usual in *Measles*, and the period may be prolonged by persistent catarrh or pneumonia. For *Mumps*, the same period from the setting in of the glandular inflammation is enough; for *Rubella*, a fortnight as dating from the outset of the eruptive stage. As a rule, straightforward cases of *Scarlet Fever* have lost their infectivity at the end of four weeks, but in this disease no criteria are known on which to base a safe opinion as to the absence of contagion then or later. It is, therefore, even at the present time, the rule to isolate cases for six weeks from onset, and for any longer period occupied by primary desquamation. This serves to cover an undue extension of the infective stage in some uncomplicated cases. Peeling of the hands and feet may be quickened by scrubbing them with a nail-brush, soap and oatmeal. Towards the end of desquamation, the feet are commonly steeped in hot water every evening; some permanganate of potash may be added. On the positive side, certain minor sequelæ are held to show a possible persistence of infectivity. Hence, in examining patients, the clinician should satisfy himself that: (A) there is no sore-throat; (B) the nose and ears are not discharging; (C) the inside of the nostrils, as far back as can be seen by ordinary inspection, are not inflamed or excoriated; (D) there are no cracks or sores about the head, including the region round the nostrils, the angles of the mouth, the folds of the ear with those behind and below it, and the scalp; (E) other parts of the skin, especially along the nails, between the toes and about the buttocks, are not inflamed or broken and suppurating. Persistent nasal and aural discharge are troublesome features when further detention is in question. Return cases are rarely referable to ear discharge after three months, but the outlook is less certain in rhinitis. In general, coincidence has to be allowed for when infection seems to arise from any discharged patient. The infection of *Smallpox* has gone by the time all crusts have separated and any sores are healed. Daily warm baths and, later, the steeping of the feet every evening in hot water, will aid decrustation. Hard masses sunk in the epidermis of the soles can be carefully detached with a blunt-pointed knife. In modified cases, with little or no crusting, the minimum period of isolation is three weeks; the mean period for average cases is about eight weeks; the maximum covers some months. In *Typhoid Fever*, isolation ends when the patient is fit to go about, and even in the acute stage it need not be stringent as regards visitors who merely come and go. The practice of examining the fæces and urine to ascertain if convalescents are carriers and should take certain precautions has not yet been generally adopted. *Typhus* cases are isolated for not less than four weeks. *Whooping Cough* seldom spreads when the spasmodic stage is definitely declining, but the safest plan is to maintain strict isolation until then, and thereafter to prevent direct contact with children until the whoop has gone.

6. **Precautions on and after Discharge.**—As the time of release approaches, patients should be in the open air every day when practicable and have a warm bath in the evening. Then a final bath is given and the hair thoroughly washed. If the disease be *Diphtheria* or *Scarlet Fever*, the patient should keep away from children for a week and sleep alone for a fortnight after discharge. After Scarlet Fever, children should not attend school for a fortnight, and for any further time required to make two months from the onset of the attack; after Diphtheria, for a month, unless the culture-test has thrice proved negative.

7. **Final Disinfection of Premises and Furnishings.**—The nurse burns valueless articles and sterilises others with a germicide or by boiling them. The local authority may remove the bedding for steam disinfection; without such treatment, the passage of time with exposure to air and light will alone render it safe in some fevers. Fumigation of the quarters is practically useless. The floor, woodwork and furniture should be thoroughly swabbed with 1 in 20 carbolic lotion and scrubbed later on with soap and hot water. It is usual to have the sick-room repainted and repapered.

II. Specific Treatment

1. **Infection,** as a method, is only represented by vaccination against *Smallpox*. Although essentially preventive in aim, it may modify the disease if performed within the first five or six days of incubation. Unless exemption is claimed under the Act in the first four months, infants must be vaccinated within six months of birth, provided they have not had Variola or are not medically certified as unfit subjects physically or owing to their home surroundings or possible exposure to infection. About one child in four is not vaccinated, and the present immunity of the country, subject at any time to failure locally, is referable to the protection of the majority, to emergency vaccination when Smallpox occurs, to the control of contacts, to care in the identification of modified cases, and to a costly system of hospital isolation. The crux of the case for vaccination is the right of its advocates to lay down the conditions under which it will do all that is claimed. These

conditions are, firstly, efficient inoculation, and, secondly, its repetition.

(A) Efficiency depends on three factors. (*a*) The lymph must give rise to the typical lesions of Vaccinia. Assuming the source to be satisfactory, there remain in question its freshness, the technique of inoculation and the clinical characteristics of the lesion. (i) Glycerinated lymph, kept cool and in the dark after issue, retains its full activity for about two months and deterioration during the next five or six is not ordinarily enough to render it inactive. If any home-stored lymph fails to infect, a freshly issued supply should be used. Even such a lymph may fail, although very rarely, and another strain can then be tried. Not until three tests with active lymph have proved negative is the subject to be regarded as immune. Three failures exempt a child under the Act. (ii) In inoculating lymph, the arm is washed with soap and water and afterwards with boiled water. Some distance below the shoulder, the lymph is spread over areas equal to the intended insertions. The areas are superficially scratched with the blunt point of a sterile scalpel or lancet in close, crossed lines. The arm being exposed to the air, ordinary lymph soon dries, but glycerinated lymph remains slightly moist and should be given half-an-hour to penetrate. Finally, a pad of aseptic gauze and wool may be bound over the part with cross-straps of oxide of zinc plaster. (iii) In three days the areas show some redness and swelling, and two days later have begun to change into vesicles. This change reaches its height on the eighth day, when the vesicles are well filled, flattened, depressed centrally, and have a red areola. Pustulation, setting in now, may be accompanied by two or three days of slight fever and axillary lymphadenitis. Maturation is complete by the tenth day. Meanwhile, redness and swelling have spread about the insertions and, exceptionally, may involve the whole length of the arm. On the eleventh day, desiccation is apparent. It ends in the formation of a crust which ordinarily comes away in the third week. The red scar blanches in time. Subsidiary vesicles occasionally develop near the primary ones, but a general vaccinal eruption is rare. Non-specific rashes, roseolar, urticarial, possibly vesicular, occur in a very small percentage of cases. (*b*) The term of immunity is directly related to the number of insertions. Four should be made, half-an-inch apart. A newborn infant exposed to Variola, or a person who is a weakling or an invalid, is acutely ill, or is suffering from some cutaneous affection, can be safeguarded for the time by one insertion. Otherwise the rule should not be varied. (*c*) The term is also proportionate to the area inoculated. Taken together, the insertions should cover at least half a square inch. As a record of efficient vaccination, besides the number and whole area of the scars, pitting is taken into account. Very smooth, superficial cicatrices suggest that the vaccinal lesions were ill-developed. In any case the scars tend to become less sharply marked with the passage of time.

(B) The protection afforded by vaccination in infancy is less persistent than that conferred after childhood ends, when it is more likely to continue in some degree through life. Consequently, revaccination at the age of twelve is requisite to maintain resistance, but all that is done in this direction in England is to make it free at the hands of the public vaccinators. In an epidemic, all adults should in any case be revaccinated whether they are contacts or not. As to the chance that a second infection may be transmitted—an issue greatly exaggerated by opponents of vaccination—for cancer and leprosy, if not tuberculosis, it may be regarded as hypothetical. Eczema may become active or extend more widely after vaccination, but its determination is less certain. Even with affections of the septic group which are readily acquired (suppurative conditions, erysipelas, impetigo, etc.), the danger is inconsiderable in view of the vast number inoculated without any untoward result. Undoubted instances of inoculated syphilis, again, are excessively rare. Under most conditions, an added infection may be merely coincident, and with the passing of arm-to-arm vaccination syphilitic infection is losing its significance even for the purposes of controversy, as, in a less degree, are the other affections mentioned. This method is therefore to be avoided, but if circumstances should make it needful, the lymph is obtained on the eighth day from a healthy subject vaccinated for the first time, and is taken from typical, unruptured vesicles. The purity of calf-lymph is further ensured by mixing it with glycerine, which greatly reduces the number of extraneous organisms or causes them to disappear. The glycerine requires time to act, and to meet this condition and the eventual loss of virulence, supplies may be dated by the makers to show the period within which they are usable. Lymph is also purified by treating it with chloroform.

2. **Vaccine Treatment.**—See article on Principles of Vaccine and Serum Treatment for various details. In *Diphtheria*, vaccine has been used to a limited extent to prevent the carrying of the bacillus or to treat actual carriers. It is suggested that the injections should begin when the local lesion is retrogressing. Hewlett and Nankivell employed a filtrate containing the endotoxin: two milligrams, doubled after a week and repeated at similar intervals if the

germs persisted. At Plaistow Hospital an autogenous vaccine of dead bacilli has been tried in a few cases: average weekly doses, 100, 200, 400, 800, 1,200 and 1,600 millions. Viewing known results, the carrying stage seems to be shortened in some instances, but the treatment may fail and its utility is not established.[1] Forbes and Newsholme tested autogenous vaccine (doses 5 millions to 400 millions) in nasal Diphtheria. The rhinitis declined, but bacilli persisted in the affected tract. Strong evidence comes from Russia, where Gabritschewski and others have inoculated many thousands of individuals with a streptococcic vaccine derived from a case of *Scarlet Fever*, that his medium is protective and of value in epidemics. It consists of concentrated bouillon culture: minimum dose, if based on age, 0·25 c.c.; maximum, 1 c.c. Three injections are made at a week's interval, the second and third doses being increased by half or doubled. Watters, treating nurses a fortnight or longer before exposure with a polyvalent streptococcic vaccine cultured from patients, in doses of 50, 100 and 200 millions at weekly intervals, observed a reduced attack-rate. Although reports conflict, it appears that autogenous vaccines may benefit patients in the acute stage. Jochmann and Michaelis advise the associated administration of antistreptococcic vaccine and serum. In carrier cases of *Typhoid Fever*, fæcal and urinary, vaccine treatment has proved disappointing, although a few successes are reported. Vaccines have been largely employed to immunise susceptibles. Wright's preparation, consisting of bacilli killed at 60° C., has, in particular, found a wide application in the protection of troops. Its efficiency is generally admitted. Two doses are injected, the first of which may be 500 millions, the second, given ten days later, 100 millions. Statistics show that the treatment lessens the chance of infection and of cases proving fatal. Besredka's method of sensitising vaccine by treating it before use with antibacterial serum applies in Typhoid Fever, and, considering experimental results, its adoption in the treatment of acute infections more generally, to produce rapid immunity and to cure, is a probable development. Broughton-Alcock has used a sensitised living vaccine in the prophylaxis of Typhoid Fever. Clinically, ordinary stock and autogenous vaccines seem to do good in doses of 50 millions, rising at intervals of three or four days to 500 millions or more. Callison has given larger doses: 500 millions increased by 100 millions every fourth day. Schäfer makes remarkable claims respecting the curative effect of his vaccine. In 150 cases he had only four deaths. There is ground for the view that a vaccine of Bordet's bacillus is serviceable in the prophylaxis and clinical treatment of *Whooping Cough.* Freeman has defined the best average dose as 100 millions. In the first year of life 25 millions may be given, in the second 50, and thereafter 100, with smaller doses of the influenza bacillus and pneumococcus, as these organisms are so constantly present and are concerned in the complicating pneumonia. To protect, the simple or compound vaccine may be injected thrice at weekly intervals, the second and third doses being doubled. Clinically, the average dose may be continued as required, week by week. In the *local affections* which complicate or follow certain fevers, as rhinitis, otitis media and cutaneous sores caused by their discharges, present results point to a useful field for vaccine treatment; such obstinate lesions may rapidly improve, quickly heal, or run a shorter course, although failure is common, particularly in otitis media. Streptococci, staphylococci, diphtheria bacilli and diphtheroid organisms are mainly found in these infections, and autogenous compound vaccines prove more effective than those from stock strains. At Plaistow Hospital no attempt is being made to separate the different germs in cultivating them: doses, 100, 200, 400, 800, 1,200 and 1,600 millions at seven-day intervals. As a general principle, the treatment should commence before chronicity is established. A vaccine of the related streptococcus is said to influence scarlatinal nephritis favourably.

3. **Serum Treatment.**—See also p. 57. In *Diphtheria,* antitoxic serum (2000 units) is given to protect contacts; its effect, said to last two, three or four weeks, is uncertain. As a curative agent, the serum is life-saving both in the faucial and laryngeal forms of the disease, and reduces the severity of non-fatal faucial cases. Nowadays heroic doses are avoided. In faucial infection with only a trace of membrane, 2000 units suffice, subject to repetition on the following day if the membrane is growing. With the tonsils partly covered on the first or second day, this dose is enough and can be repeated in twelve hours. When they are entirely covered, 4000 units should be given on the first or second day, and the same dose after the above interval; if two days have passed or there is nasal discharge, 6000 units are repeated. Should the membrane spread in these instances, a third dose is indicated. With thick membrane covering a wider area than the

[1] Scholtz' application so far promises better than vaccine treatment. A 24 hours' broth culture of s. aureus is sprayed on the throat every two hours or less frequently. The diphtheria bacillus may disappear quickly. Septic infection is unusual and nearly always slight. The broth may be swabbed as well as sprayed on to the mucous membrane.

When children are carriers, hypertrophied tonsils and postnasal adenoids may require removal.

tonsil, but not the palate extensively, 6000 units repeated twice are usually sufficient, unless nasal discharge is marked or the fourth day is reached, when 8000 units are required. This last is now the regular maximum dose for all severe cases in any stage, but if there be much palatal exudate it is sometimes raised to 12,000 units. In laryngeal cases, 8000 units are given twice or thrice at twelve-hour intervals, according to the degree of obstruction and the amount of membrane in the pharynx. Although early administration is needful to obtain the full effect of the serum, the dose has to be greatly increased as time passes, and after some days little or no benefit is said to accrue from its use, the writer does not care to withhold antitoxin so long as any membrane is present. Antitoxin saves some early cases of diphtherial croup from operation, and with operation has reduced the case-mortality to about 1 in 3, much better results than this being obtained in some series. Acute diphtherial rhinitis, rare as apart from faucial infection, is treated with maximal doses if severe. Sub-acute and chronic rhinitis is a common sequel of the acute form, and diphtheria bacilli are not rarely present in the nasal discharge following Scarlet Fever. If antitoxin has already been used in the former instance, its repetition is contra-indicated; otherwise, and in the latter, moderate doses may reduce the discharge, but this effect is apt to be transient and serves chiefly as an adjunct to vaccine treatment and local antiseptics. Diphtherial conjunctivitis, an uncommon infection, usually shows quick improvement under antitoxin treatment. Large doses should be given if membrane forms, or the eye may be destroyed; fatal cases are recorded. Wound diphtheria responds to antitoxin. Chronic diphtherial dermatitis, oftenest impetiginoid in its features, is commonly very resistant to non-specific treatment, whereas antitoxin promptly clears up some cases and improves others. In *Scarlet Fever* with a frank septic element, antistreptococcic serum in large doses (50 c.c.) appears now and then to be useful, but its action is unreliable. Cumston, employing a polyvalent serum prepared by means of streptococci from cases of the disease, considered the results favourable. The efficacy of other special serums (Marmorek's, Moser's, Aronson's) has not been proved beyond question. The value of serum taken from convalescents and of diphtheria antitoxin in Scarlet Fever and *Typhoid Fever* is doubtful. In the latter fever, ordinary antibacterial serum has been supposed to confer a passing immunity. Curatively, it is a failure. Chantemesse states that the case-fatality of the disease has been reduced to less than 5 per cent. by his special serum, given in doses of a few minims, repeated once or twice. Wright is of the opinion that it may act as a vaccine. Macfadyen and others prepared an anti-endotoxic serum, which is the medium, in theory at least, likely to prove effective. Hewlett also adopted this method of preparation; the serum did no apparent harm and seemed to influence the disease favourably. Forssman's and Ludke's limited observations with doses up to 50 c.c. bear this out. Lieuriaux' serum for *Whooping Cough* was stated by him to be beneficial; the same claim has been made for serum from convalescents. Serum from vaccinated heifers has been injected in *Smallpox;* also that obtained from convalescents. Their effect remains in doubt.

III. Treatment by Chemical Germicides

Local antiseptic applications (see Part IV) seem sometimes to influence septic infection, but their effect on the specific lesions of the fevers is inconsiderable, that of faucial *Diphtheria* being a possible exception. By the mouth, salol (10 gr. four-hourly in fine powder) renders the eruption of *Smallpox* less foul and markedly reduces the cutaneous irritation in many instances during the developed stage and decline. Haller has administered salvarsan in four cases and advises its early use to modify the rash. Prescribed internally in the specific bacilluria of *Typhoid Fever*, urotropin (10 gr. thrice daily in an ounce of water) sterilises the bladder in less than a week, and most cases of actual cystitis are quickly cured; but if bacilli of the colon type are present in the latter affection, it may resist the treatment. When given for bacilluria, the drug is continued for ten days. It causes a fall in the number of bacilli in chronic urinary carriers, but there is an increase when it is withheld. Two apparent cures in which borovertin was prescribed are reported.

IV. Local Treatment

It will save space to state here that in the treatment of certain local lesions (rhinitis, otitis media, cutaneous sores) the principle is to employ agents that are antiseptic, astringent and stimulating. As a rule, irritation is avoided, and as the response varies with the case, the strength of a given application may have to be altered or another agent chosen. When improvement ceases, it is often advisable to change the treatment. Again, two applications may be used alternately, each for a few days. In chronic cases, all stimulating applications should be stopped after a time to ascertain whether they are not acting as irritants and prolonging inflammation.

1. **The Mouth.**—In severe cases of fever, the nurse cleanses the teeth, gums and tongue after the two-hourly feeds during the day with

some such mixture as the juice of a lemon and an ounce each of glycerine and peppermint water. For simple, aphthous and mild ulcerative stomatitis the mouth may be swabbed every four hours with undiluted glycerine of borax. If there is definite ulceration, it should be first syringed with a saturated solution of boracic acid; in painful cases, with 1 in 40 carbolic lotion, which the patient, however, must not swallow. Or, where pain prevents both syringing and swabbing, a spray of carbolic solution (1 in 20) may be substituted. Ulcerative stomatitis of the destructive type is an occasional complication of *Septic Scarlet Fever* and occurs, more rarely, in *Measles, Typhoid Fever* and *Typhus*. It is usually treated by syringing with chlorine water. To make this, five drachms of powdered chlorate of potash are placed in a large stoppered bottle and fifty minims of strong hydrochloric acid added. Chlorine gas is given off and displaces the air. In small quantities at a time, with frequent shaking, thirty ounces of water are poured into the bottle to make the solution. If the ulcers continue to spread, they may be touched with carbolic acid while the patient is under ethyl chloride. Gangrenous areas may have to be scraped and stippled over with strong nitric acid. Open-air treatment is indicated in such cases.

2. **The Fauces and Pharynx.**—Sore throat is met with in most of the fevers: as the local lesion of *Scarlet Fever* and many cases of *Diphtheria*, and, with varying severity, as a regular or occasional feature of *Measles, Rubella, Smallpox, Typhoid Fever, Typhus* and *Whooping Cough.* In all forms of tonsillitis and pharyngitis a very common prescription is—

℞ Tinct. Fer. Perchlor. ♏ x
Glycerin. ♏ x
Aq. ad. ʒ ii

thrice daily or four-hourly for a child of four. The writer prefers to exclude chlorate of potash from this formula. As a local application when the affection is mild, with little or no discharge, tablets containing formaldehyde offer a convenient means of treatment if the patient is not a young child; one is allowed to dissolve in the mouth every two hours during the day. Sucked drugs are, however, contra-indicated when there is much discharge. A gargle may be sufficient for catarrhal cases after childhood—

℞ Formalin. ♏ i
Aq. ℥ ss;

Liq. Pot. Permang. ♏ x
Aq. ℥ ss;

Acid Carbol. Liq. ♏ ii
Glycerin. Borac. ♏ x
Aq. ad ℥ ss;

or—

Hydrogen. Perox. Liq. ʒ ss
Sod. Chlorid. gr. ii
Glycerin. ♏ xv
Aq. ad. ℥ ss

To control infective discharge, to prevent the patient from swallowing it, to minimise sepsis, and to make respiration less difficult when there is faucial and nasal obstruction, the throat is syringed four-hourly or thrice daily with boracic lotion. No other method is so cleansing, and the statement that it may cause otitis media is not borne out by comparative observations at Plaistow Hospital, where the nurses are taught to syringe very gently. An irritable child or older delirious patient may resist the treatment, and so put undue stress on the heart or exhaust himself; or the fluid may be swallowed or dyspnœa induced or increased. Thorough swabbing every two or four hours during the day is then substituted. The gargling solution of peroxide of hydrogen (see above) may be prescribed for this purpose, or—

℞ Formalin. ♏ x
Glycerin. ʒ i
Aq. ad. ℥ ss;

Acid. Carbolic. Liq. ♏ iii
Glycerin. Borax. ʒ i
Aq. ad. ℥ ss

Solut. Hydrarg. Perchlor. (1 in 4000).

If swabbing is barred for the same reasons as syringing, the medium containing formalin or carbolic acid may be sprayed on the throat instead at like intervals. Subacute or chronic tonsillitis, especially a sequel of *Scarlet Fever*, may also be treated by swabbing or spraying with one of these media or a marked astringent:

℞ Glycerin. Alum. ♏ xxx
Aq. ad. ℥ ss

Indolent, enlarged tonsils ought to be removed. Destructive ulceration, which may involve the palate and is a danger in septic *Scarlet Fever*, requires the same treatment as noma of the mouth (par. 1). If chlorate of potash is prescribed locally for the affections included in this and the previous paragraph, it should not be continued too long, as it is itself an irritant.

3. **The Nose.**—Acute rhinitis, besides being present in a slight or marked form in nasal *Diphtheria* and frequently in septic *Scarlet Fever*, is, in its milder catarrhal phase, specific to *Measles* and *Whooping Cough.* The objects of treatment are to get rid of the infective matter, to render breathing more easy, and to discourage sepsis. The nose is never syringed, as such treatment may induce otitis media, and it is questionable if even gentle

douching is safe. The best application is a very strong, coarse spray, two-hourly during the day at first and less often as the affection subsides. When there is much ulceration and foul discharge peroxide of hydrogen is one of the best agents to employ; otherwise nothing is better than formalin (see above). Chronic rhinitis is one of the most troublesome and obstinate affections in hospital practice, chiefly seen in children after *Scarlet Fever*, and not rarely after *Diphtheria*. Local treatment improves most cases, but although the discharge is reduced, congestion and swelling, with or without slight ulceration, are apt to persist, and further progress is then slow. As a rule, the writer begins treatment with a spray of formalin or peroxide of hydrogen. When response ceases, it is replaced by the following—

℞ Cupri. Sulph. gr. ii
Aq. ad. ℥ ss

Should this fail in effect, either from the start or after a time, an ointment is substituted—

℞ Ichthyol. gr. ii
Vaselin. ℥ ss.

This is inserted as far up the nostrils as possible with a cotton-wool swab made on the end of an eyed probe. Even so weak a preparation is at times too irritant; on the other hand, its strength may have to be increased, and in some cases the curative effect is remarkable. Vaccines may be used.

With the cessation of discharge under any treatment, zinc ointment is used if the mucous membrane remains congested, and, finally, boracic ointment or vaseline. Children may have to wear check-splints to prevent picking of the nostrils. Epistaxis is rather common in *Typhoid Fever* and may be due to vascular stress in *Whooping Cough*. It may then be stopped by spraying a little adrenalin into the nostrils. Again, it may depend on ulcerative rhinitis. In such cases, and when it is a sign of toxic changes in the vessels or, generally, is difficult to control, the nasal passages may have to be plugged via the nostrils with strips of lint smeared with boracic ointment. Its arrest is important in severe fever.

4. **The Ear.**—Otitis media is a characteristic complication of *Scarlet Fever*, fairly common in *Diphtheria*, less so in *Measles* and *Typhoid Fever*, and rare in *Mumps* and *Rubella*. In the early, painful stage, the meatus is syringed with warm boracic lotion every four hours and two minims of tincture of opium, mixed with three minims of olive oil, dropped into it from a warm spoon. A pad of wool, heated at the fire, is applied over the ear. When perforation threatens, myringotomy should be performed, but requires an expert, particularly if the patient be a young child. Syringing is continued after a discharge sets in, and in this stage, urotropin (4 gr. in water four times a day for a child) may bring rapid improvement. When infection spreads to the antrum, an incision is made to the bone to avert mastoidectomy, or at least to postpone it if possible if the patient is not yet convalescent from the primary fever. But if, as is the issue in a minority of cases, relief does not follow, and general disturbance referable to the local lesion is sustained, this or the radical operation is called for. Meningitis, thrombosis of the transverse sinus and cerebral or cerebellar abscess, are rare developments, for which the cranium is opened. Chronic otitis, usually ensuing on acute infection, ranks with rhinitis in the frequency with which it resists treatment and detains patients in hospital. The writer relies mainly on absolute alcohol to cure such cases. Success depends largely on the alcohol reaching the middle ear in quantity, and doing so undiluted. Hence, the ear is first syringed out with 10 per cent. peroxide of hydrogen solution to loosen and bring away crusts and clear out the discharge. With the ear dependent, the solution is then thoroughly dried out of the ear with pointed spools of absorbent wool. The alcohol is dropped into the meatus from a warm spoon and the tragus pressed very gently several times to aid its passage beyond the drum. The patient lies with the ear uppermost for five minutes, after which the alcohol is allowed to gravitate out. The application is repeated every night and morning, and in due course a full week's rest from all treatment is given to ascertain if the discharge, having become scanty, will stop. Vaccine treatment may be used.

5. **The Eye.**—Mild conjunctivitis, such as is usual in *Measles* and may complicate *Scarlet Fever*, etc., nearly always subsides quickly when a four-hourly moist boracic dressing is applied without pressure over the orbit. The same affection, in a more intense form, is specially frequent in *Smallpox*, and is treated through the acute stage by washing out the sac, at least every four hours while the patient is awake, with a mild antiseptic solution such as boracic lotion. The lotion is squeezed out of a piece of aseptic gauze. The lids are prevented from adhering by an ointment of boracic acid and vaseline (1 in 40). If conjunctivitis in any of the fevers becomes purulent, nitrate of silver solution (10–15 gr. to the ounce) should be painted on the inner surface of the lids every twenty-four or forty-eight hours until retrogression is assured. In subacute or chronic inflammation which does not yield rapidly to boracic dressings, it is advisable to dispense with drops, and to apply the same solution (5–10 gr. to the ounce). Corneal ulcer, occurring in *Smallpox*, is an

indication for the instillation of atropine (4 gr. to the ounce) unless the lesion is not only peripheral but is tending to perforate. The conjunctival sac may require constant cleansing. In keratitis, atropine is instilled and warm boracic fomentations applied.

6. **Glandular Structures.**—Adenitis, centred behind the angles of the lower jaw and showing in degree a fairly regular relation to the severity of the local lesion, is common in *Diphtheria* and *Scarlet Fever* and occasional in *Measles*. In the latter two diseases, boracic fomentations are applied, in the first, cotton-wool. In all, if there is much pain, the skin may also be painted with glycerine of belladonna. Abscess (very rare in *Diphtheria*) is opened by a small incision in line with the jaw, drained with a tube, and syringed out at each time of dressing. In chronic adenitis, primary or as a sequel to the acute form, the skin may be painted with iodine and syrup of iodide of iron prescribed. Given suitable conditions, much time should be spent in the open air. Necrotic subcutaneous cellulitis is a dangerous complication of the above fevers, although rare in Measles. The overlying skin is incised at several points when breaking down has commenced, and the tract well irrigated with one of the emulsifying germicides (1 in 40) every four hours. Boracic fomentations are applied early and continued while the skin and contiguous tissues are sloughing. Open-air nursing seems to favour recovery when the lesion is not too extensive, but the case-fatality is very high. The parotitis and other glandular lesions of *Mumps*, including orchitis, are treated with boracic or belladonna fomentations; the septic parotitis complicating *Smallpox*, *Typhoid Fever* and *Typhus* with the former, plus an incision if abscess occurs. According to Tirard, ichthyol and lanoline (equal parts) is an excellent dressing in *Mumps*. Chronic enlargement of the bronchial glands is one of the sequels of *Measles* and *Whooping Cough*. Treatment: Syrup of the iodide of iron, a liberal diet and open-air conditions.

7. **The Intestine.**—Febrile disturbance of this tract is accentuated by the ulcers of *Typhoid Fever*, but is considered as a general question later on, as the ulceration is probably unaffected by drugs. Two accidents due to it, however, require prompt treatment.

(A) *Hæmorrhage.*—The care taken in moving cases of Typhoid Fever is increased when blood shows in the motions. More or less continuous loss of blood, referable to oozing, is generally treated with turpentine: 20 minims every four hours. It is given in capsules, or a drachm of it is placed in a bottle with two ounces of milk and one-half of the white of an egg, and this emulsion slightly sweetened; the bottle is well shaken when a dose is administered. At intervals, especially if there is much diarrhœa, an opiate enema may be ordered: Tinct. Opii 20 minims in $1\frac{1}{2}$ oz. of starch mucilage. The diet of milk may be iced and reduced by half for a time. To still the heart, control restlessness, lessen peristalsis and protect from shock, the writer gives morphia ($\frac{1}{6}$ gr.) at once in the more sudden form of hæmorrhage if it is at all severe. Over the abdomen are placed small pieces of ice on a single layer of lint with its four edges pinned round rolls of cotton-wool which take up the water as the ice melts. Any trickle from the rolls is kept off the flanks by squares of batiste or jaconette, the upper edges of which are secured under the lint. The patient's lower limbs are kept warm by an extra blanket and a hot-water bottle. Food may be stopped for twelve to twenty-four hours, the patient merely receiving sips of water; on the following day, iced whey may be temporarily substituted for milk. Up to a certain point, a drift towards heart-failure is not counteracted as clotting is desired, but when syncope becomes the immediate issue, stimulating measures cannot be avoided. The patient is covered with relays of warmed blankets, if necessary, the foot of the bed raised, and salt solution (one to two pints, or even more) injected either subcutaneously or by venous puncture. Alcohol, camphor, strychnine and oxygen may also be employed.

(B) *Perforation*, apart from diagnosis and laparotomy within twenty-four hours, is practically always fatal. Morphia should be withheld until the question of an operation is decided. The details of diagnosis need not be discussed here, but it may be noted that pain, although often slight, is the most valuable sign, since it calls attention to the possibility that perforation has occurred. The other early and most reliable indications are quickened breathing and shrinking or disappearance of the hepatic dulness. The last sign is generally undervalued. Its significance depends largely on a daily examination of the area in cases likely to perforate and an hourly one from the time perforation is suspected. The main surgical points are that ether should be given by the open method; that the operation should be rapidly performed; that the peritoneal cavity should be cleansed by swabbing, and not washed out with saline solution unless peritonitis is already extensive; that gauze wick should be used for drainage in early cases, as against a tube for those in which the douche is employed; that the gauze should be removed in thirty-six hours as adhesions form; and that a saline infusion (one to three pints) should be given immediately after the operation and again in twelve hours. The patient having had salt solution, food can be discontinued for eight hours and then half an ounce of peptonised

whey given every half-hour for twelve hours. The whey is gradually increased to five ounces two-hourly, on the second and third days; then mixed with milk, which soon replaces it entirely. The recovery rate is said to be about 1 in 3, but many fatal cases are probably not recorded. In *peritonitis without perforation*, the writer keeps the patient free from definite pain by injections of morphia (say, $\frac{1}{6}$ gr. every twelve hours or less often) so long as tympanites is not developing. Hot fomentations or turpentine stupes are applied to any specially tender area.

8. **The Heart and Blood-Vessels.**—(A) In the writer's experience, no treatment affects favourably the purpuric lesions which mark the grave hæmorrhagic type of certain fevers (e.g. *Diphtheria, Smallpox*). (B) The myocarditic changes which are a factor in febrile heart-failure and occur in an extreme degree in some cases of *Diphtheria*, *Scarlet Fever* and *Typhoid Fever* are covered as to treatment by Part VI. of this section. (C) Endocarditis, while less rare in *Scarlet Fever* than other acute infections here considered (*Diphtheria, Measles, Mumps, Smallpox, Typhoid Fever, Typhus*) is by no means common in that disease despite the frequency of murmurs. The so-called simple form grades into the still rarer ulcerative type which is hardly ever frankly pyæmic. (D) Phlebitis, most often affecting the femoral region, is a frequent late complication of *Typhoid Fever*. The limb is raised on a pillow and bandaged from the foot with a domette roller; it should be kept still until the acute phase is past, although pyæmic infection is excessively rare. If there is pain, belladonna fomentations are used. The patient may, owing to continued œdema, have to wear the bandage for some weeks or even months after getting up, but in nearly all cases it ultimately subsides.

9. **The Respiratory Tract.**—See also article on treatment of the nasal passages.

A. The *Larynx.*—(*a*) Laryngitis is often present in early *Measles;* less frequently during its full development or decline. It occurs sometimes in *Whooping Cough*, may complicate septic *Scarlet Fever*, and is common in confluent *Smallpox*. The patient is placed in steam or uses a steam-inhaler if there is obstruction. In rare instances tracheotomy is required in the last two fevers for severe stenosis. The same is true of *Measles*, but here a further issue arises: as time passes in the incidence of croup, there is a greater chance that it is diphtherial, and the rule in all late cases is to give antitoxin without waiting for the bacteriological examination. The ulceration peculiar to *Typhoid Fever* may be present without symptoms, and very rarely indeed calls for surgical relief. In severe fever generally, slight but persistent obstruction may be an indication for operation. (*b*) The treatment of laryngeal *Diphtheria* has been placed on a new footing by the improved prognosis due to the success of antitoxin. Early cases are placed in steam, and oxygen may also be administered, especially at night. In this way, with antitoxin treatment, some patients are saved from operation. The need for the latter is mainly judged in young children by the degree of thoracic recession. Owing to the greater rigidity of the costal arch at and after the age of six, cyanosis and the state of the pulse gain relatively in importance. Rapid tracheotomy with a small incision is practised in hospital. The inexperienced, however, will find the ordinary operation easier, and should, if there is no time to follow it in detail, begin with the full-sized incision. Opening the trachea, as compared with intubation, is suitable for all cases, whereas the latter operation is contra-indicated when there is much naso-pharyngeal obstruction, faucial inflammation is of the ulcerous type, the patient has or has recently had Measles, or immediate asphyxia threatens. Also tracheotomy is not so difficult in the absence of special experience and offers the nurse a better chance of postponing fatal suffocation if acute obstruction returns and the medical attendant is not within call. It alone should be used in private practice. Intubation, again, gives less trouble than tracheotomy as regards preparation, the actual operation, and, especially, the subsequent nursing; is justified at an earlier and therefore more favourable stage of stenosis; and has a lower death-rate, probably under 30 per cent. at the present time. Patients should be nasally fed with peptonised milk for at least a fortnight if a tracheal tube is worn so long, and always while a laryngeal tube is in place. The writer strongly advocates the use of steam in all cases of tracheotomy, as, even with extensive broncho-pneumonia, death after the operation is in most instances directly due to gradual obstruction of the lower trachea and adjacent bronchi by inspissated discharge, and its development cannot be foreseen. The nursing of tracheotomy cases should be on strict aseptic lines.

B. *The Lower Respiratory Passages.*—The treatment of *bronchitis*, as regularly present in *Measles*, *Whooping Cough* and severe *Smallpox*, very consistently in *Typhoid Fever*, and incidentally in septic *Scarlet Fever* and *Typhus*, does not call for comment except in relation to the two first-named diseases, in which the occurrence of lobular pneumonia, especially among young children, is the chief clinical fact. (*a*) From the onset of *Measles* the patient is kept strictly in bed and should wear a woollen undervest. The head of the bed being screened to keep off draughts, there should be very free ventilation,

and, if compatible with it, an air-temperature of 65° F. In the early, dry stage of the catarrh, a good all-round prescription is—

℞ Vin. Antimonial. ♏ ii
Spirit. Æth. Nit. ♏ v
Liq. Ammon. Acet. ♏ xx
Aq. Camph. ad. ʒ ii

four-hourly for a young child. When this phase passes—

℞ Vin. Ipecac. ♏ v
Syrup. Scill. ♏ viii
Glycerin. ♏ v
Aq. ad. ʒ ii

also four-hourly. If bronchitis becomes marked, a steam-kettle is required; if dangerously suffocative, oxygen should be given. Should older children develop the capillary form, with glutinous secretion—

℞ Ammon. Carb. gr. ii
Ammon. Chlorid. gr. ii
Tinct. Seneg. ♏ iv
Syrup. Tolu. ♏ xxx
Aq. ad. ʒ ii

every four hours. The patient gets up when all signs of bronchial trouble have disappeared, and when the weather is fitting should be much in the open for some weeks after convalescence; he should also be well fed and not too thinly clad. Lobular pneumonia is, as a rule, a direct outcome of the acute bronchitis, but sometimes sets in during convalescence. (*b*) Treatment of the initial catarrh of *Whooping Cough* is on the same lines, but the danger of early lobular pneumonia is less as it is more specially a complication of the ensuing spasmodic stage. The spasms, though nervous in origin, are related to the severity of the enduring catarrh, each, doubtless, tending to maintain the other, a fact implying that treatment should be directed against both. At the outset, as in *Measles*, the freest ventilation should be secured, and its continuance is important in cases severe enough to be kept in bed during the spasmodic stage; secondarily, a temperature of 65° F. is desirable. In warm weather open-air treatment is best. Frequent vomiting due to the paroxysms may seriously affect the nutrition, and early in such cases the patients should be given some predigested food (*e. g.* Benger's) immediately after the seizures. Response to medicinal treatment on the part of the paroxysms is variable; a drug which benefits one case may fail in another. The prescription containing ipecacuanha and squill (see above) may be continued after the whoop sets in; to it a bromide or belladonna may be added, or they may be prescribed alone—

℞ Sod. Bromid. gr. ii
Tinct. Bellad. ♏ ii
Glycerin. ♏ viii
Aq. ad. ʒ ii

four-hourly for a child aged four. The pushing of belladonna is widely favoured—

℞ Tinct. Bellad. ♏ iii
Spir. Chloroform. ♏ iv
Aq. ad. ʒ ii

every four hours, the tincture to be increased with each dose until the pupils are dilating and thereafter continued with caution. Bromoform relieves some severe cases. Owing to its pungency it should be freely diluted. As a poison which tends to sink in mixtures, it is best prescribed in separate doses: 4 minims with 10 minims of rectified spirit in an ounce of water four-hourly at the age of four. Antipyrine has many advocates: 1 gr. cautiously increased to 2 gr. thrice daily for a child of four. Oxygen is used in very severe paroxysms; also a little chloroform by inhalation. When the spasmodic stage is unduly prolonged—

℞ Quinin. Sulph. gr. ii
Acid. Hydrobrom. Dil. ♏ v
Syrup. Aurant. ♏ xv
Aq. ad. ʒ ii

three times a day for a child of four. The removal of enlarged tonsils and adenoids may also be indicated. Exposure to cold air may favour persistence, which is unfortunate in view of the need for free ventilation. Most children, being up in the paroxysmal stage after a time, can be out of doors in the middle of the day if there is a convenient garden and the air is not too cold or dust-laden. On recovery, the general health should receive the same attention as after an attack of Measles.

C. *The Lungs and Pleura.*—(*a*) Lobular pneumonia may develop in septic *Scarlet Fever.* If there is coughing when fluids are taken, the patient is, unless rhinitis prevents, fed with the nasal tube. For broncho-pneumonia itself, as also when it complicates laryngeal *Diphtheria* and severe *Smallpox*, ammonium carbonate (5 gr. for an adult, 1–2 gr. for a child) may be prescribed four-hourly in milk. In the first of these diseases it is useful when tough discharge is obstructing the lower trachea and main bronchi after tracheotomy. Multiple cases of lobular pneumonia in hospital should be nursed as units, since there is reason to believe that the pneumonic affection may spread from one to another. In all cases of lobular pneumonia the patient's position in bed should be frequently changed. As the cause of so many deaths from *Measles* and *Whooping Cough*, it requires special consideration, and

here open-air treatment is entitled to the first place. Discrimination is, however, necessary as regards the exposure of individual patients to cold air. Particularly in *Whooping Cough*, cases not doing well in the open may improve on removal to a warmed room or ward. Through the warmer months of the year nearly all cases can be treated continuously in the open air, whereas when it is chilly at night some are better within doors at this time. The writer does not favour out-door treatment in winter. If cases are kept indoors owing to a low air-temperature or because there are no facilities for outside treatment, very free ventilation is essential. All patients should wear a cotton-wool jacket. When the bronchitic element is marked, ammonium carbonate is of great service in many cases; the chloride may be combined with it (see B). Stimulation is begun before weakness of the heart has become very marked; alcohol may be given first and continued if supplementary agents have to be employed. For high temperature, patients are tepid-sponged. A warm bath with a cold douche to cause deep breathing and so more fully aerate the lungs in cyanotic cases, is recommended by some authorities; the method is more suited to hospital than private practice. Oxygen should be administered when cyanosis begins to tell on the heart. A liberal and nutritious diet, suitable to the individual case, is important, owing to the tendency to asthenia and emaciation and the long period of fever. (*b*) The common liability to *hypostatic congestion* in *Typhoid Fever* and *Typhus* is counteracted by placing a pillow partly under the body on each side alternately in order to raise the level. The congestion may deepen to a low form of pneumonia in which cardiac stimulation, open-air treatment, and oxygen from the onset of cyanosis are chiefly to be relied on to save life. (*c*) *Lobar pneumonia* is met with now and then in *Measles*, and occasionally also in *Typhoid Fever;* it is rare in *Diphtheria*, *Scarlet Fever* and *Whooping Cough*. (*d*) *Pleurisy* and *empyema* are exceptional or rare complications of certain fevers.

10. **The Skin.**—(A) All but the gravest cases of fever are washed from head to foot between blankets every night and morning. In *Chickenpox*, *Smallpox* and *Typhoid Fever* an emulsifying disinfectant may be added to the water (1 in 100). (B) The irritation of the *rash* in *Chickenpox*, *Smallpox*, etc., is partly allayed by sponging the skin with 1 in 40 carbolic lotion. Salol largely controls it in the second disease. In both, to prevent laceration by scratching, the hands may be loosely enveloped in lint bags, tied about the wrist with tape. Even then children may have to wear check-splints to save the face from friction. Owing to the presence of variolar pocks on the arms, the splints are at times applied over lint spread with vaseline. Patients at all ages should have their nails closely trimmed. A warm bath (96° F.), besides favourably influencing the febrile disturbance of *Smallpox* in selected cases, is soothing to the skin; one may be given in the evening, or, as a recognised method of treating the disease, thrice daily or four-hourly. There are also good reports of the continuous bath. Iced compresses lessen pain caused in the hands and feet by the eruption. Even women's hair is cut short if the rash is profuse on the scalp. Maturation, so far as the writer's observations go, is not definably modified by any local application or by red light. To lessen pitting, however, Welch and Schamberg recommend the painting of the face once or twice a day with tincture of iodine if tolerated, as is usual, from the outset till about the tenth day of the rash. Rockhill, using 10 per cent. of iodine in glycerine, confirms their findings. Throughout an attack of Chickenpox, and in Smallpox when incrustation is established, if not sooner as mentioned above, patients should have a daily warm bath. If deep ulcers form in *Chickenpox*, open-air treatment should be adopted where possible, the patient well fed, and a tonic prescribed. (C) *Boils* and *abscesses* (*e. g.* in septic *Scarlet Fever*, *Smallpox*, *Typhoid Fever*) are fomented and incised. Widespread abscesses of the skin, perhaps metastatic, are a rare feature of septic *Scarlet Fever*, and require the same treatment. (D) Bedsore is generally a result of carelessness in the nursing of *Smallpox*, *Typhus* or *Typhoid Fever*, but may result from a previous skin affection or from boils or abscesses. The nurse sees that the bed under the patient is kept smooth, and moves him carefully to prevent friction. In Typhoid Fever he is regularly turned partly on one side and then the other, to vary the areas of pressure. The chief point, however, is to keep the back dry and to save it from the irritating effect of urine and fæces. Any evacuation is washed off at once with soap and water and the soap removed with pure water. The skin is then well dried, dabbled over with methylated spirit, and powdered with equal parts of zinc oxide and starch. If the skin becomes inflamed, it is the nurse's duty to report without delay. In such cases frequent diarrhœa and incontinence of urine are the usual cause; to render the skin relatively "water-proof" and improve its circulation, it is gently massaged with lanoline. The patient may be placed on a water-bed and pressure kept off the part by a ring-pad, which is also used when an ulcer forms. The latter, cleansed if necessary by first applying a charcoal poultice, is dressed with red lotion. (E) *Cutaneous sores in the acute stage of fevers and*

as sequels.—Apparently because of the desquamation, patients suffering from *Scarlet Fever* are specially liable to sores, and these may also form in any fever characterised by a local discharge, notably *Diphtheria.* The skin about the mouth, nostrils and ears is most often affected. Largely as a phase of prophylaxis, the fever nurse is expected to avert the formation of sores even when discharge is copious. When washing the patient, she is careful to cleanse the skin thoroughly and dry it well; where the discharge emerges, the adjacent skin is thickly smeared with lanoline. Children are apt to scratch themselves owing to the irritation and may so start sores or hinder healing. Their hands may then be muffled (par. B). In hospital, as a more effective method, check-splints are applied. These are slips of cardboard, lightly bandaged to the front of the elbows, and allow the patient to bend his arms slightly but not to touch the face. The treatment of actual sores is bound up with that of the lesions from which the discharges come, a question dealt with elsewhere in this article under various heads; in chronic cases it includes the use of vaccines. The sores are cleansed with a boracic fomentation and dressed with zinc ointment, copper sulphate solution, or, as a very useful all-round application, ammoniated mercury ointment mixed with as much vaseline.

11. **The Urinary Tract.** — (A) Albuminuria complicates most fevers at times, either in the acute stage, when it may be transient or persist in convalescence, or as a passing or chronic sequel. In *Diphtheria*, *Scarlet Fever* and *Typhoid Fever* it is frequent. When marked in the febrile stage, fluids are given very freely, and the loins poulticed if the urine becomes scanty. The patient wears a woollen nightdress and broad flannel belt. Abundant fresh air is needful; in summer, under proper conditions, the patient's bed may be placed out of doors. Liq. Ammon. Acet. (1 dr. four-hourly in milk or a mixture) may be prescribed from the outset, even in the severest cases, and Spirit. Æth. Nit. (15 m. for an adult) added if the decline is slow. A laxative should be given daily, or less often as required; severe purgation is, in the writer's opinion, undesirable. If, with a normal temperature, the albumen has not disappeared after ten days, and the patient's general condition is satisfactory, boiled fish can usually be included in the diet. In more chronic cases, fluids should be given in quantity, and perchloride of iron may be prescribed thrice daily. Protein food is restricted, but not unduly. Following four weeks of stationary albuminuria without fever, the patient can generally be allowed up, given that the amount of albumen is not large. In any event, it does not benefit chronic cases to keep them in bed indefinitely; marked improvement or recovery may quickly follow when they are permitted to go about. Fresh air seems to aid recovery; suitably clothed, such patients need not as a rule be kept within doors in warm, dry weather. Should the albumen persist for, say, two months, and particularly if there is only a trace, the effect of cantharides is worth trying: half a minim thrice daily, increased progressively to three or four minims within a fortnight. It should be discontinued, or the dose reduced, if the albumen increases. (B) *Nephritis,* uncommon or rare in other fevers, including *Chickenpox, Diphtheria, Smallpox, Typhoid Fever, Typhus* and *Whooping Cough,* is the most characteristic complication of *Scarlet Fever,* in which its incidence, with infrequent exceptions, is confined to the convalescent stage. The early treatment of its acute phase is the same as in albuminuria (see above). Firstly, however, to maintain the flow of urine is a more salient point, since uræmia lies ahead as the chief danger to life. Water is pushed and may be given by the rectum as well as orally. Large poultices are applied to the loins at once and continued until the decline is well advanced. Secondly, while it has been suggested that vomiting may be eliminative, and that it should not be too readily discouraged, it is the writer's practice to stop it as soon as possible. Thirdly, strong purgatives are commonly given and repeated. It is the writer's experience that harm may be done by pushing such treatment; at the same time, the bowels have to be kept open, and smart purgation serves an end in exceptional instances of extensive œdema or when this condition affects the lungs. Fourthly, sweating is induced, if need be by steam or hot-air baths, and here again the writer prefers the middle course to extreme treatment. Fifthly, the patient lies between blankets, wears a woollen nightdress and also a broad flannel belt when poulticing is stopped; exposure of the body to cold air is avoided. Uræmic symptoms make more urgent the necessity for keeping up the flow of urine: especially so, as most cases are not in actual danger for more than a few days, and what is almost a crisis usually follows: a marked increase in the output of urine and quick general improvement. Whiffs of chloroform will mitigate severe convulsions, during which the breathing may be freed by holding the jaw forward and securing the tongue with forceps, while a cork is kept between the teeth to prevent the latter from being bitten. Cyanosis due to convulsions may be a factor in heart-failure, and specially indicates the use of oxygen. No case, at any age, should be allowed to die without blood-letting as a last resource: from three to five ounces are taken from a child, up to fifteen

ounces from an adult. If, in the course of recovery, the nephritis eventually becomes more or less chronic, tincture of cantharides may be tried with the reservations already noted.

The other treatment recommended for prolonged albuminuria applies to persisting nephritis, but patients are kept longer in bed, especially in winter. When they are up, and for some time after the disappearance of blood and albumen from the urine, the question of exposure to cold, and therefore of clothing, remains important. (C) When cases of *cystitis* in *Typhoid Fever* resist urotropin, the bladder may be washed out once daily with boracic acid solution (20 gr. to the ounce). For chronic cases resisting this treatment a 2 per cent. solution of argyrol may be substituted. *Retention*, common in *Typhoid Fever* and *Typhus*, and not very rare in other acute infections, is favoured by the recumbent position. Children, unless too ill, should be seated in a warm hip-bath, which seldom fails to act; if the bath cannot be used, a large fomentation is applied over the lower part of the abdomen. Urotropin is given when the catheter has to be passed in Typhoid Fever. (D) *Vaginitis*, a rare complication of *Scarlet Fever*, etc., will usually yield quickly to a daily douche of argyrol (10 per cent.), replaced after four days by perchloride lotion (1 in 5000).

12. **The Nervous System.**—Early and adequate doses of antitoxin lessen the incidence of paralysis in *Diphtheria*, and its severity when it occurs. From the first symptom—usually a nasal voice—the patient is kept lying down. Nasal feeding is begun at once if a food-cough develops. Strychnine is generally prescribed; some give it in minimal doses (*e. g.* $\frac{1}{500}$ gr. every eight hours, hypodermically), while others push it within the safety limit. Neither statistically nor clinically has the writer been able to make sure that it modifies the course of the paralysis, and this statement also holds for galvanism, which is begun later. He is not in favour of allowing patients with mild and stationary paralysis to sit up in bed, since there is ample evidence that trivial forms of exertion may aggravate or prolong the affection. In the declining stage his patients do not sit up until the last sign of paralysis has disappeared. Involvement of the respiratory muscles is always grave. The bed is tipped up at the foot; oxygen may also be given for cyanosis and to relieve distress, but as a means of saving life it has proved disappointing. So-called paralysis of the heart, a late disturbance, sometimes associated with the peripheral affection in its severe form, and seen typically as a paroxysmal weakening of the circulation accompanied by other symptoms, is very dangerous and demands direct stimulation.

13. **Bones and Joints.**—(A) The *osteo-periostitis* of *Typhoid Fever* may or may not go on to suppuration, and is treated accordingly with fomentations or by incision, which suffice for most cases. (B) *Non-suppurative arthritis*, peculiarly frequent during the decline of *Scarlet Fever*, is treated like mild acute rheumatism. (C) Suppurative arthritis, a rare feature of septic *Scarlet Fever*, yields as a rule to incision and washing out with an antiseptic solution. Apart from associated general infection, the prognosis in cases so treated is on the whole remarkably good, both as regards survival and recovery of the joint.

V. The Treatment of Fever, chiefly in relation to Cardiac Weakness

Acute microbic intoxication is considered under this head in its graver phases. Therapeutically, its pyrexial element is brought into undue prominence by the term "fever"; the salient feature from this standpoint is not a rise in temperature, which may, indeed, be absent, but cardiac enfeeblement; when death results from fever *per se*, gradual heart-failure is nearly always the mode, and treatment is largely directed from the first against this drift towards syncope. It is not to be expected that medicinal measures will antagonise, as a whole, a form of poisoning so complex. Although they are often useful, dependence has largely to be placed on others which sustain resistance to infection, while extrinsic factors directly or indirectly depressant to the circulation are minimised if they cannot be obviated. As regards depressing factors, cardiac debility tends to increase despite all available means of treatment, and it is proportionately important to recognise that this weakness is readily and often quickly induced, whereas recovery of the lost ground is usually slow and may be impossible. Finally, even main indications cannot all be met in many critical cases, and life may then depend on a timely recognition of what is essential in treatment.

1. **Dieting.**—(A) Without referring in detail to experimental facts as to the relation between nutrition and resistance to infection or between the former and cardiac efficiency as observed clinically, it may be said that to give food proper in kind and sufficient in quantity is the first rule of treatment; that in dieting fever cases, digestive disturbance is more readily determined or aggravated than checked; and that, in respect of quantity, practice must often fall short of principle. As formal pudding, fish and meat diets do not figure in the treatment of marked fever, they may in their general application be dismissed with the statement that the first, or even the second, is commonly given in the acute stage of mild cases; that in

severe cases a pudding diet is usually begun when the decline is established; that fish is added in these cases early in convalescence; and that fish partly gives place to digestible forms of meat in three or four days. This course can be followed in *Scarlet Fever* without an increased incidence of nephritis. The gradation to a full diet in *Typhoid Fever* is carefully regulated. When decline is certain and the appetite returns, the patient can have cocoa, chocolate and weak tea to drink; also junket and Benger's food two or three days later, with egg-custard and milk-jelly for a change, and bread-crumb, light sponge-cake, bread-and-milk and milk puddings, in the course of the first week of convalescence. At the beginning of the next week, in the average case, boiled white fish may be allowed with a suitable vegetable in small quantity; in the following four days, boiled sweetbread and stewed tripe; at the end of the week, chicken, minced at first. *Milk diet.*—The drawbacks to cow's-milk as a complete diet need hardly be discussed here, nor need methods used to soften the curds, or make them less coherent or smaller, be described. Such treatment of milk is indicated when there is nausea, vomiting or diarrhœa, and always if undigested curd appears in the stools. For particular cases of gastric disturbance it may be advisable to skim the milk lightly. Lactose or glucose (1 oz. to the pint) is sometimes added to raise the carbohydrate content, but increased intestinal fermentation may result. If milk is given over a long period in *Typhoid Fever*, salt should be administered in it, or, as recommended by Ker, liberally in beef-tea. When a fever occurs in infancy, dieting has a special importance, as vomiting and diarrhœa are common at this time and frequently dangerous (*e. g.* in *Measles*). In the first six weeks of life, one part of milk and two of water are given to fever patients: total amount of the mixture for twenty-four hours, 18 oz.; in the second six weeks, equal parts: total amount, 24 oz.; in the next four months, one part of water and two of milk: total amount, 24 to 36 oz. The last dilution serves up to the age of one year, with an increase to 44 oz. Thereafter, with exceptions in the case of children just past infancy, one part of water may be added to five parts of milk at all ages, unless it is desired to use the milk as a vehicle of extra water. Young children receive 36 to 48 oz. of the actual milk; older ones 48 to 60 oz.; adolescents and adults, from 60 to 80 oz. Only for those suffering from inanition when first seen, taking insufficient milk, or showing a tendency to emaciation during a long attack of fever, need this diet be supplemented by raw egg, beef-tea, meat extract, cream, a standard proprietary food, etc., according to age, the state of digestion, and the presence or absence of idiosyncracy. *Milk substitutes.*—Occasionally milk, however treated, is rejected or ill-digested. In its place, Benger's food made with water and, possibly, a little cream, may then be given. (B) The experimental fact that the withholding of *water* reduces resistance to one infection is probably true for all. Besides this reason for giving an adequate amount in severe fever, there are others which point to the advisability of pushing it: notably, the tendency of the urine to become scanty. Milk, as regularly diluted (see above), provides the minimum quantity; more may therefore be added to it or ordered as a beverage (lemonade, imperial drink, orange water, apple water); the total for an adult suffering from one of the longer fevers (*Smallpox*, *Typhoid Fever*, *Typhus*) with oliguria reaches six pints. (C) *Methods of feeding.*—Milk diet is divided into two-hourly feeds during the day, and four-hourly ones at night, so that an adult receives respectively five ounces and ten ounces at a time. The intervals should be maintained unless the milk is peptonised. If the spasmodic vomiting of *Whooping Cough* is interfering with nutrition, the patient is fed immediately after the paroxysms with pre-digested milk and concentrated foods in small quantities. Because of distaste for food, pain on swallowing, tonsillar swelling, irritability, delirium, marked dyspnœa or coma, insufficient nourishment may be taken by the mouth, and the nasal tube—an instrument which probably saves many lives—is then generally used; eight ounces of peptonised milk are given every four hours to a child of four. Rhinitis, with obstruction or epistaxis, may prevent nasal feeding, and what is taken by the mouth may then be supplemented by suppositories, rectal injections, or both (see below).

2. The Prevention and Control of Vomiting.—The initial vomiting of *Diphtheria*, *Scarlet Fever*, etc., has rarely any prognostic significance, but that this is a leading issue in cases of late sickness is indicated by the fact that there is a loss of both food and water, rest is disturbed, and physical exhaustion is at times induced. Primarily, the cause has to be dealt with. When it is local the addition of a drachm or two of whisky or brandy to a nauseating drug or to food may act as an antemetic. Otherwise treatment is mainly dietetic. Milk may have to be altered or replaced by one of the temporary foods mentioned below. In the worst cases the stomach requires rest, and nourishment is administered *per rectum*. Peptonised milk, unboiled after preparation, is given every four or six hours to the amount of four or six ounces, according to the interval. If this is not retained, peptonised meat suppositories may be ordered every four or six hours with saline

enema or infusion (one pint) every morning and evening. If even iced water has been rejected by the stomach, an attempt should be made to give it again in twelve or twenty-four hours. When tolerated, the quantity is cautiously increased, and in due course the water is replaced by albumen water, peptonised whey or white wine whey. Raw meat juice and champagne may be tried; also small doses of a beef-tea or extract so prepared as to have some nutritive value—low at best. Where, in cases less grave, treatment can be begun with such foods, the necessity for progressing to a complete food should be constantly in view. Meanwhile, very dilute whisky or brandy may be included in the diet. "Late vomiting," as a strict term, is applied to the obstinate sickness which sets in very frequently in *Diphtheria*, and now and then in other fevers, when the heart has become markedly degenerated if not dilated. As the critical period approaches in the disease named, care should be taken not to start vomiting by the use of purgatives, other drugs or some change of diet; whether so determined or spontaneous in its onset, its arrest is one of the most difficult and vital problems in the treatment of Diphtheria. As a rule all measures fail, but Ker states that it may sometimes be checked by hypodermic injections of morphia and atropine. Coghlan recommends—

℞ Atropin. Sulphat. gr. $\frac{1}{100}$
Strychnin. Hydrochloride gr. $\frac{1}{100}$
Solut. Adrenalin. Chlorid. (1–1000) ♏ v
Aq. ♏ x

hypodermically every four hours. The author would exclude strychnine from this prescription. Given alone, it is ineffective if not harmful. The view that atropin may act beneficially is strengthened by Dr. G. C. Garratt's observations in a few cases treated on somewhat original lines. He advises the early administration of belladonna by mouth. If vomiting continues, nothing is to be swallowed, but the patient fed every 4 hours by enemata, each containing 20 to 30 minims of tinct. belladonnæ. Twice in 24 hours 20 gr. of potassium or sodium bromide are to be added. These doses are for a child of 3 or 4. An hour after the bromide the patient is wrapped in a large towel. The operator spreads a mackintosh on his knees and takes the child's head between them while the nurse holds the body and legs. The mouth being sufficiently open, a good-sized œsophageal silk-gum tube is passed rapidly. When the resulting disturbance has subsided, water at 115° F. is poured in. At first the water is rejected, but the stomach becomes more tolerant as it fills. Enough must be given—10 to 12 oz. The tube is withdrawn quickly but cautiously and the patient taken to bed with the utmost gentleness after a due interval. Rectal feeding is continued and, if all goes well, the bromide first reduced gradually and then the belladonna. The tube feeding is repeated every 12 hours and some bland food leaving no curd substituted for the water, *e.g.* somatose. The writer has seemingly saved an occasional case by giving oxygen for ten minutes every hour. Oxygen and infused saline solution are always worth trying in persistent febrile vomiting, with poulticing of the loins if a uræmic element is diagnosed or suspected.

3. The Prevention and Control of Diarrhœa.—The reasons for treatment are the same as in vomiting, danger being greatest when young children are affected. A mild purge to clear the intestine, and, afterwards, a laxative to ensure a daily motion if there is constipation, are routine measures in fever cases, but the writer regards drastic purgation, especially after the initial stage, as rarely advisable. Dieting may mitigate or stop diarrhœa (see pars. 1 and 2). Beef-tea or peptonised milk may cause it, and have to be withdrawn. In the putrefactive diarrhœa of fevers as a whole, antiseptics are more serviceable than astringents. Combining the qualities of both, and first in all-round value, is bismuth salicylate: 4 gr. in mucilage of acacia, 20 minims with water to 1 drachm for a child of four, thrice daily or every four hours; or 2 gr. with an equal dose of salol, may be prescribed in the same vehicle. If such signs as pallor, pinching of the face and a small, weak pulse, show that the loss of water is prejudicing the circulation, salt solution should be infused; as a method of giving water, infusion also remains when it is rejected by mouth and rectum, as may be the case in *Measles* and toxic *Scarlet Fever* accompanied by vomiting and diarrhœa, or when there is vomiting and rectal intolerance without diarrhœa. In *Typhoid Fever*, chlorine water has a long-standing reputation in the control of severe diarrhœa; allowance being made for its slow action, it is a useful preparation: the dose is ½ to 1 oz. every four hours, and may contain 1 to 2 gr. of quinine. If a quicker result is desired or the chlorine does not act in four days, salol (10 gr. finely powdered, every four hours) or beta-naphthol (10 gr. thrice daily in cachet) may prove effective.[1] Should such agents fail: tincture of opium, 5–20 minims, according to age, may be given as an enema in 1 to 2 oz. of starch mucilage, not to be repeated within twelve hours. Statistics

[1] Tincture of iodine (3–4 min. thrice daily) has been praised in the treatment of *Typhoid Fever*, but as it is also recommended for *Typhus*, its effect may be partly general, since the febrile disturbance of the two diseases present common features.

show that there is a better average chance of recovery when patients are constipated in this disease, for which the writer never uses even a laxative. Constipation is relieved by enemata every day or second day.

4. **The Control of Abdominal Distension.**—Generally, distension is taken to signify some modification of diet, and is thus controlled indirectly. It may, however, threaten to embarrass the circulation and breathing (*e. g.* in *Typhoid Fever* and the broncho-pneumonia of *Measles* and *Whooping Cough*), and has then to be treated more promptly. Turpentine may be ordered by the mouth : 5–15 minims every four hours, in keeping with the patient's age and the condition of the kidneys; the latter may prevent its use, and an intestinal antiseptic (see above) have to be substituted. From two drachms to one ounce of turpentine may also be given in a pint of starch mucilage as an enema and ice applied to the abdomen.

5. **Ventilation.**—That an abundant supply of fresh air is beneficial in febrile disturbance, and may lessen the chance of heart-failure by sustaining vitality is, in the writer's opinion, proved by clinical observation. This result is most obvious in the open-air treatment of *Typhus ;* such treatment has been extensively employed for Typhus alone, but the writer believes that its common adoption for selected cases of many other acute infections is only a matter of time. Its utility in local respiratory affections is beyond question. Unfortunately, as a secluded verandah is necessary in a private house, it is rarely feasible under home conditions, but should in most cases be approached as nearly as circumstances allow. Cross ventilation should be secured if possible, and the windows kept wide open except in cold weather, when inlets can be provided by opening them at the top and closing the lower sashes on ventilating boards, while a fire is used for the removal of foul air *via* the chimney.

6. **The Avoidance of Chill.**—As indicated by coldness of the surface of the body, and especially of the extremities, undue chilling may have an adverse influence on the circulation when it is already weakened by fever; moreover, such added depression tends to persist, for example, in *Diphtheria.* This, however, is rarely an obstacle to free ventilation; for, although in the above disease, and in *Measles* and *Whooping Cough*, a temperature of 64° F. is best, the breathing of warmed air must be considered a minor question in comparison with the proper clothing and covering of the patient and the use of hot bottles when necessary. If, through careless nursing, a severe case of fever becomes chilled, warmed blankets should be tucked round the patient, hot bottles placed near the feet, and stimulation pushed.

7. **The Relief of Forced Breathing.**—The reference here is not to the gross occlusion of the air passages characterising diphtherial croup, but to its presence in a minor degree as a result of nasal and faucial obstruction or slight œdema or ulceration of the larynx, mostly met with as complications of septic *Scarlet Fever.* Frequently, the continued effort affects the weakened heart, and may mainly determine the unfavourable course of given cases. Timely tracheotomy may then save life.

8. **Æration of the Blood.**—Even when slight, cyanosis is not a sign which can be safely neglected if the heart is weakening. In some instances, swelling and the collection of discharge in the naso-pharynx may be the cause, in others, laryngeal obstruction, bronchitis, lobular pneumonia, hypostatic congestion, lobar pneumonia. Local treatment of the nose and throat, or feeding by the mouth, may have to be discontinued because they cause respiratory distress or make children resist or hold their breath. Whatever other treatment is adopted under the heads cited, oxygen inhalation is beneficial. When the cyanosis is associated with hypostatic congestion or lobular or lobar pneumonia, it is an indication that the heart should be stimulated.

9. **The Maintenance of Renal Excretion.**—As bearing on treatment, it is significant that febrile urine is abnormally toxic, and that a rough proportion exists between the severity of the typhoid state as observed in diseases with a long febrile stage (septic *Scarlet Fever*, *Typhoid Fever*, *Typhus*, etc.), and the quantity of urine passed. In such cases, and also in *Diphtheria*, the urine should be measured and charted every twenty-four hours. The early and continued administration of water in addition to that contained in milk, is the first step in their treatment. In the fevers generally, and specially in Diphtheria, as the result of a specific process, the lessened output of urine results, in part at least, from loss of vascular tonicity, aided by cardiac weakness in many cases. If the deficiency becomes a danger, the methods of increasing the urine in scarlatinal nephritis apply, but improvement of the circulation may be the main consideration. The good effect of hydrotherapeutic treatment in suitable cases (par. 10) is largely attributable to constriction of the vessels and a consequent increase in the urine excreted.

10. **The Control of Pyrexia.**—The theory that pyrexia is merely an expression of resistance to infection does not negative the treatment of a high sustained temperature as far as may be safely possible, since the relation between it and some nervous forms of febrile disturbance is such that its reduction is often desirable, and it seems

directly to affect the heart even when it does not amount to hyperpyrexia. However, the effect obtained, particularly in improvement of the circulation as against its depression, should decide the question of further treatment, continued or occasional. The very young, those past middle age, and some who have heart disease, are not good subjects for active or prolonged hydrotherapy, while bathing is contra-indicated in *Typhoid Fever* if there is hæmorrhage or limited peritonitis, or, obviously, perforation is suspected or has been diagnosed. It is better, again, when drugs are prescribed for their antipyretic effect, to reserve them for conditions in which a temporary fall is desired or hydrotherapy has to be supplemented; they are neither safe nor reliable agents for producing more than a passing modification of the temperature.

(A) *Sustained Treatment.*—(*a*) The *continuous bath* is mainly used for *Typhoid Fever* with a high average temperature, and is life-saving, but should not be attempted without special apparatus. Patients are immersed for days at a time, the temperature of the water varying, inversely with that of the patient, between 90° and 98° F. This bath is also beneficial in severe *Smallpox.* (*b*) The *continuous pack* serves for similar cases of *Typhoid Fever* and when hyperpyrexia is feared. The patient wears warm stockings to the knee, and over them a blanket is tucked. From knee to neck, with the arms outside and bandaged in cotton-wool, he is closely covered with a wet sheet taken from water at 90° F. More water at the same temperature is dribbled on to the sheet from a sponge as evaporation occurs. If there is depression, the added water may be at 98° F., but in any case the treatment has often to be stopped owing to the effect on the heart. (*c*) *Ice.*—High temperature, more particularly when associated with cerebral excitement, as is frequent in *Typhus* and occasional in *Typhoid Fever*, may, after the hair has been cut very short, be treated by suspending an ice-bag over the patient so that it lies lightly against the head, or by applying an ice-cap or, preferably, an aluminium cap of Leiter's tubing served with iced water. Ice-bags may be placed along the upper part of the spine and in the axillæ and groins when the temperature keeps in the neighbourhood of 105° F. As a matter of comfort rather than to reduce temperature, patients may be covered with an ice cradle in warm weather. (*d*) *Diaphoretics* are largely prescribed for the discomfort associated with a high temperature and dry skin, notably when there is also a dry catarrh of the respiratory tract (*e. g.* in the first stage of *Measles* and *Whooping Cough*); but, although even hyperpyrexia may occur when the skin is moist, it seems that sweating induced by drugs may aid the imperfect control of pyrexia by the nervous system. The latter effect is most apparent in the case of young children—

℞ Pot. Cit. gr. v
Spir. Æth. Nitros. ♏ v
Liq. Ammon. Acet. ʒ i

for a child of four; hourly for four doses, then every four hours.

(B) *Periodical and Incidental Treatment.* (*a*) The *gradual bath* is the most effective agent in treating hyperpyrexia, one of the gravest developments of *Typhoid Fever*, etc. When the temperature is 106° F. or more, what chance there may be of saving life usually depends on an immediate and marked reduction. If, therefore, the danger has not been foreseen and a bath kept ready, during its preparation the patient should be wrapped in a sheet saturated with cold water. At this time, or whenever he is in the bath, he should receive ten and five grains respectively of quinine and phenacetin with an ounce of brandy or whisky, not too dilute. The temperature of the bath is at first 100° F., and is lowered by pouring in cold or iced water at the foot, while the warmer water is bailed out at the other end. Shivering and mental distress are ignored, but the pulse has to be frequently noted, as collapse is possible. On removal from the bath when the rectal temperature has dropped to 101° F. or, as the limit of the treatment, in half-an-hour, the patient is given half an ounce of whisky or brandy and dried with friction. Children are least subject to hyperpyrexia, and can be given a cold or tepid pack, with quinine and alcohol in doses suitable to their age. (*b*) The *repeated bath* has its greatest vogue in the treatment of severe *Typhoid Fever*, given either every four hours or when the temperature reaches a stated level, such as 103° F. The cold bath (65° F.) is now less favoured than the warm one (80° F.). Evidence is abundant that these baths reduce the average mortality of the disease. (*c*) *Tepid* and *cold packs* replace graduated, tepid and cold baths when the latter are contra-indicated or cannot be provided. For a tepid pack the temperature of the water is 85° F., for a cold pack, 65° F. or less; iced water may be used in the hyperpyrexia of adults. They are given, in the same way as the continuous pack (see above), for thirty minutes, an hour, or longer. (*d*) *Hot sponging*, having as its object the dilatation of the superficial vessels to cool the blood in quantity, is employed when the temperature rises towards 105° F., and the circulation is so depressed that cold or tepid applications do not induce a favourable re-action. Its success and safety depend on the

use of water as hot as the patient can bear with comfort, and its completion in four minutes. Except as regards the lower extremities, the patient as a rule is afterwards only covered with a sheet for half-an-hour. The fall in temperature is apt to be transient. The great flexures are not sponged. (*e*) *Cold* or *tepid sponging* is the favourite method of reducing temperature in *Typhoid Fever*, etc. Cases may be sponged for twenty minutes at set intervals or when 103° F. or some other point is touched. The sponge, or, in hospital, lint square, is applied with special thoroughness to the great flexures and along the spine. In cold sponging, the extremities, from the knees and elbows, are excluded.

11. **The Securing of Rest and Sleep.**—The improvement frequently observed in the pulse of grave fever cases after sound sleep is the only point which need be mentioned to define the bearing of this issue on heart-failure. To obtain a quiet sick-room, other requirements may have to be sacrificed in a noisy house or neighbourhood. The lighting of the room is another factor; apart from cases of extreme irritability, active delirium, meningism and meningitis, it is ordinarily better, while protecting the eyes with a screen, to admit daylight freely, unless the patient is definitely somnolent. In the quiet of the night, sleep is less likely to be disturbed. Moreover, treatment and nursing is arranged to give as long intervals of rest as possible at night—a matter demanding the close attention of the clinician, and one to which many statements in this article are relevant, especially as regards the suspension of particular methods of treatment, and, in some instances, the substitution of others, and also the control of affections which interfere with rest and sleep; *e. g.* vomiting, diarrhœa, cough, dyspnœa, cutaneous irritation, pain, pyrexia. Free ventilation favours sleep. For broken rest at night, the patient may be sponged in the evening with hot, tepid or cold water and given a hot drink. If sponging fails and the temperature is high, phenacetin (2 gr. for a child of four; 10 gr. for an adult) may be prescribed in addition, with or without alcohol. The last (1–2 drachms of brandy or whisky for a young child, ½ to 1 oz. for an adult) has special value as a soporific when there is great cardiac and general debility. It is more likely to act when the patient is an abstainer and is not having regular doses, and should be given in hot water, but not highly diluted. Simple treatment on these lines is apt to fail in definite insomnia, such as is common in toxic *Scarlet Fever* and *Smallpox*. The tepid pack may then succeed, if not contra-indicated by depression. Generally, hypnotics are required, and may be supplemented by the above measures. For all-round use: veronal, 2–10 gr. according to age, in hot milk. If it fails—

℞ Paraldehyd. ʒ iii
Extract. Glycyrrh. Liq. ʒ ii
Syrup. ℥ ss
Aq. ad ℥ iii

1 oz. for an adult, and less in proportion for a child, repeated once or twice at intervals of an hour if the patient does not sleep. Veronal (2–8 gr.) aids its action and may be prescribed with the second dose if the first has no effect. For persistent sleeplessness in children's cases—

℞ Syrup. Chloral ♏ xv
Sod. Bromid. gr. v
Aq. ad. ʒ ii

as a draught at the age of four with a drachm of whisky or brandy and half an ounce of water. When insomnia is a dangerous element in fever, and continues for, say, four days in spite of other treatment, morphia remains as a potent agent, not always safe, yet one which does good service in many cases, and seems sometimes to avert death: $\frac{1}{12}$ gr. hypodermically in later childhood, $\frac{1}{6}$ gr. for an adult. The early repetition of a dose is not advisable; if sleep is not caused in an hour, veronal (2–10 gr. according to age) will usually induce it.

12. **The Control of Delirium.**—Active delirium, most frequent in *Typhus*, toxic *Scarlet Fever* and *Smallpox*, mainly affects adults. Exhausting in itself, it disturbs sleep and is commonly accompanied by insomnia. Quietness is important in its control, and for this reason noisy cases should be separated. Its other treatment includes the application of an ice-bag or Leiter's tubes to the head, packing, sponging, and the administration of such drugs as are noticed above as useful in insomnia—preferably paraldehyde, with morphia for obstinate cases. In Smallpox and Typhus, patients may have to be watched; they may try to get out of bed, and have escaped from isolated quarters. Rarely, they are dangerous to themselves or others. Some have to be restrained by tying their wrists and ankles, wrapped in cotton-wool, to the side-rails of the bed with short lengths of bandage. In passive delirium, the chief indications are to secure sleep, if possible without drugs, and to support the heart.

13. **The Discouragement of Stupor and Coma.**—Deep stupor and coma—the latter specially a feature of *Typhus* and not uncommon in severe *Typhoid Fever*—react unfavourably on the heart. Their direct treatment is unsatisfactory, and reliance is rather to be placed on the early adoption of measures which tend to aid resistance to infection, to lessen intoxication as by keeping up the flow of urine, and to maintain the circulation. Strong black coffee (5 oz.

thrice daily) may be ordered in coma and oxygen administered for ten minutes every hour. The advisability of bleeding plethoric patients should be considered, particularly if the acute stage is nearing its end.

14. The Control of Convulsions.—As a febrile manifestation, convulsions may occur in infants and young children at the outset of various fevers, and end in heart-failure. A mustard bath should be given; if the seizures are prolonged and embarrass the breathing, chloroform in small quantity, oxygen continuously.

15. The Relief of Pain.—While acting directly on the circulation if severe, pain in various degrees tends to exhaust and to disturb sleep; when persistent, it cannot be ignored in serious cases of fever, even though it is slight. In particular cases, hot applications, counter-irritation, or a local or general anodyne may be required.

16. The Arrest of Hæmorrhage.—Bleeding, when insufficient in itself to be fatal, may still count as a factor contributing to the heart-failure of cases already critical, as occasionally happens in naso-faucial *Diphtheria* and often in *Typhoid Fever*. Prompt treatment in such cases may be vital. On the other hand, there are instances in which marked toxic symptoms improve after spontaneous hæmorrhage in Typhoid Fever. As a therapeutic measure, bleeding is adopted in uræmia, the pulmonary œdema of nephritis and in certain cases of pneumonia and coma.

17. The Avoidance of Elevation.—A striking feature of recent treatment in febrile cases is the care taken to keep the head low when there is vascular relaxation and the heart is acting feebly. Pillows are often dispensed with, the head resting on a soft, folded towel; a noticeable improvement in the pulse may ensue when this position is maintained, and the reverse result obtained if the head is raised. Sudden death has become rare in *Diphtheria* and other fevers, since patients have been systematically prevented from sitting up. The effect of this movement, however, need not be actual fainting with death as a possibility: in the vast majority of cases it is revealed by pallor and quickening of the pulse, which also loses volume and may become irregular or show increased irregularity. Slight as the change often is, the mischief wrought in a very short time may thenceforward be traceable in the course of a case towards recovery or death. Restless children may have to be kept down with a restraining belt, properly designed to allow movement without becoming displaced.

18. The Avoidance of Muscular Exertion.—Muscular stress is detrimental to the weakened heart even when the patient is lying down, and its effect may persist. Accordingly, methods of treatment and feeding may have to be altered or stopped in the former instance if they are resisted. Food, etc., should not be left where patients suffering from cardiac debility can reach out for them.

VI. The Bearing of Treatment on Related Forms of Febrile Disturbance

It is evident that direct and indirect relationships exist between local phases of the febrile state. One may intensify another, or there may be a mutual influence of this kind, while in some instances a single phase may be linked with several. Such processes could only be presented comprehensively as aspects of clinical pathology, but a recognition of the more important ones is implied in various methods of treatment embodied in the preceding pages. As a general fact, such interdependence, while often dangerous if ignored, has its favourable side for the therapeutist, since treatment effective in one direction may lead to a wider improvement. For this reason, the timely appreciation of the factors chiefly making for heart-failure in given cases and the most effective, if often indirect, methods of controlling them, is of great importance. It must be added that circulatory weakness may itself be concerned in certain processes which in turn tend to accentuate it; *e. g.* persistent vomiting, dyspnœa, hypostatic congestion of the lungs, renal efficiency, insomnia.

VII. The Direct Treatment of Cardiac Weakness

In the progressive weakening of the circulation, the question when stimulation of the heart should be commenced is often difficult to decide. The statement just made, however, points to the danger of undue delay, and it may be said that vicious circles involving the circulation generally call for the use of stimulants if the related processes cannot be alone effectively treated. In this connection, although to give alcohol before it is needed, and especially to push it prematurely, is objectionable, it is as a rule the drug first to be prescribed when stimulation will probably be necessary for more than a few days, and has the advantage that it can usually be continued later on if other agents are employed. For severe *Diphtheria* it may be ordered in the exudative stage, and is sometimes used for weeks thereafter. Its success as a stimulant depends on two conditions: the dose must be sufficient, the dilution not too great. Thus, in order to increase the dose, it may be better to prescribe it four-hourly rather than at shorter intervals; also, the amount of water, milk, etc., added to brandy or whisky should, if possible, not be more than 5 to 1. Four-hourly doses: 20 minims to 1 dr. for an infant, 1–2 dr. in the following years,

2–3 dr. in later childhood, $\frac{1}{2}$–1 oz. for adults. Always, the effect produced is the guide to further treatment: a fuller pulse, steadied more or less if irregular, not materially quickened and possibly slowed, indicates that alcohol is benefiting the patient, and that enough is being given. The minimum effective dose is the proper one, and it is only in exceptional instances that those mentioned have to be exceeded. Champagne, acting more transiently, may be ordered every two hours. It replaces brandy and whisky when these cause nausea or are rejected. Strychnine ranks with alcohol as a cardiac stimulant: $\frac{1}{150}$ gr. or less for an adult, $\frac{1}{300}$ gr. or less for a child, by hypodermic injection thrice daily or four-hourly, with $\frac{1}{60}$ gr. as a single dose in the former case, proportionately reduced in the latter. Firstly, however, in useful doses, it may have to be stopped after a few days because muscular twitching begins. Secondly, apart from its obvious toxic action, it may in the end affect the heart unfavourably; the pulse may improve on its withdrawal. While it has a deserved reputation for cardiac degeneration, the fact that it is a vaso-constrictor has to be taken into account when the heart is dilating. It is of special service in hypostatic congestion and extensive inflammatory affections of the lung as met with in the fevers. A third stimulant of value is camphor in the form of Curschmann's solution—two parts dissolved in three parts of sulphuric ether and seven of olive oil: 10–15 minims four-hourly for an adult, 5–8 minims for a child; 20–30 minims as an emergency dose. Having rarely to be stopped owing to restlessness and other mild toxic symptoms, it can be prescribed for several days continuously, either alone or with strychnine, or as a substitute for the latter if it is discontinued. Adrenalin (4–8 minims of a 1–1000 solution hypodermically every four hours) has been chiefly employed to sustain the circulation in *Diphtheria*, and the improvement observed at times to result in that disease is probably not comprised in a rise of blood pressure alone. Its administration should be commenced in severe cases when the local lesion is declining, if not sooner. Because of a possible rise in blood pressure, caution is required in its use when the heart is markedly degenerated and dilated. The theoretical advantage of strophanthus in the cardiac debility of fever is not realised in practice. Digitalis more often does harm than good. However, when a crisis is approaching, and particularly in lobar pneumonia at a late stage, it may be useful: 5–8 minims of the fresh tincture thrice daily or every four hours, the pulse being watched and the urine measured. The rapid infusion of normal salt solution has a place in the treatment of cardiac failure: average amount, one pint. A glass funnel or other container is hung over the patient to hold the solution, at a temperature of 105° F. to allow for cooling. The fluid passes by gravitation through a rubber tube and large-sized antitoxin needle into the subcutaneous tissue of the anterior axillary fold. Finally, oxygen, every half-hour, hour, or continuously, remains for cases which respond but slightly or not at all to other measures. Its administration should not be postponed until the patient is almost moribund.

VIII. Treatment during Convalescence

Cases lightly covered in the pyrexial stage (as in *Typhoid Fever*) may require more bedclothes when convalescence sets in; a cotton or linen nightdress may have to be changed for a woollen one. Adequately clothed and protected against draughts, most mild cases of any fever but the above may sit up in bed through the acute stage. Also excepting Typhoid Fever, patients after a straightforward attack of average severity can usually sit up on the fourth day of convalescence; in Typhoid Fever, on the tenth day at the earliest, and possibly not until some time in the third week. Following severe febrile disturbance in general, the interval depends chiefly on the state of the heart. While signs of degeneration persist or the pulse is markedly quickened or slowed, or remains irregular, permission to sit up is withheld. The most dangerous stage of faucial *Diphtheria* being nearly always post-febrile and frequently subsequent to the disappearance of the membrane, in severe attacks of this disease the patient may have to be kept lying down for many weeks, quite apart from the supervention of paralysis. The period during which patients sit up may vary from a day or two to a fortnight or longer, according to the general condition and the state of the heart. In *Chickenpox* they are ordinarily allowed to get up when it is apparent that no more vesicles are forming, and those last out have desiccated; in *Measles*, after the acute stage is ended and catarrh has disappeared; in *Rubella* when the temperature is normal and the rash has faded; in *Typhoid Fever* and *Typhus* when the patient can sit up in bed for the greater part of the day without tiring, and, in the former, the ulcerated intestine has had time to heal (see above); in *Diphtheria*, when the heart has recovered. Even mild cases of *Scarlet Fever* are better in bed for three weeks after the onset of illness, as the period during which nephritis is most likely to develop is then covered; this rule is followed at Plaistow Hospital. For *Smallpox* the time varies greatly. The mildest cases of Varioloid, without secondary fever, can be up when the character of the rash

becomes certain; on the other hand, after a confluent attack it is sometimes several weeks before a patient is strong enough to rise. When they first leave their bed, fever patients may have to spend some days, up to a week, or even longer, on a couch. In *Diphtheria*, *Scarlet Fever* and *Typhoid Fever*, lingering heart-weakness without obvious symptoms under rest conditions is not rare. However, pallor and slight dyspnœa on exertion may suggest its presence, and in some instances there is accentuation of the second aortic sound, irregularity, a short or weak first sound, reduplication, systolic bruits. Sudden deaths after supposed complete convalescence from *Typhoid Fever* and *Diphtheria* are on record, but are extremely rare; the ordinary result of permitting patients so affected to go about too soon is that their general health remains unsatisfactory. A good red wine at meals for adults, a tonic such as Easton's syrup, or for children, Syr. Fer. Phos. Co., and, in due course, a change to the country or seaside, are all beneficial to those who have recently recovered from a severe attack of fever. The last is specially indicated in *Measles* and *Whooping Cough* when debility persists or children are of poor physique. J. B.

INFLUENZA

Any attempt to lay down a general scheme of treatment to include all the various forms which influenza can assume would be an impossible task; but there are certain measures which seem to have met with general acceptance. Although universal approval cannot be regarded as infallible proof of the value of a particular line of treatment, it is interesting to find that since the sixteenth century the debilitating character of the disease has been looked upon as its chief danger. It was this which moved so ardent an advocate of venesection as Sir Thomas Watson to say that "the chief risk of mistake is that of being too busy with the lancet. Certainly those affected by this disorder do not well bear active depletion." Influenza is indeed best met with patient inactivity on the part of the victim, whilst the doctor takes the rôle of gaoler. In any epidemic of influenza, the fatal cases occur amongst those who struggle against the disease. Those who give in soonest get up earliest and suffer least from the after-effects. The most important part of the cure is that the patient must promptly go to bed. There is no merit in resistance; *cedendo victor abibis*. Experience warns us that the patient who insists on going about during the early stages of the disease is a danger to every one he meets owing to his virulent infectivity, and is adding to the perils which he himself will presently encounter. Prophylaxis against influenza appears to be impossible. The immunity conferred by an attack is very short-lived. Neither age, social station, nor environment offers any protection when the epidemic is abroad: with the sole exception that the suckling infant escapes. Even eucalyptus, camphor and other like "odoraments to smell to" do not save their votaries. In an ordinary mild attack characterised by sudden onset of pain in the back, aching limbs, eyes and head, with a rise of temperature to 101 or 102° F., no further treatment may be necessary than that the patient should go to bed and take a mild diaphoretic mixture to which may be added salicylate of soda—

Liq. Ammon. Acet ʒ ii
Sod. Salicyl. gr. x
Syr. Zingiberis ʒ i
Aq. Chloroformi ad ℥ i

every four hours.

Aspirin (Aceto-Salicylic Acid) is an excellent alternative: it may be given four-hourly, either in cachets (10 gr.), or in a mixture with mucilage of tragacanth. Salicin (10 gr.), Novaspirin (Methylene-citryl-salicylic acid) (10 gr.) and Salophen (acetyl-para-amido-salol) (10 gr.) are useful drugs of a similar kind. The ammoniated tincture of quinine, although often credited with almost specific powers, seems to be quite inert and incapable of relieving any of the discomforts of influenza. In fact, quinine in any form often adds a tinnitus of its own to the patient's sufferings. There is one exception, namely, quinine salicylate (5 gr.), which may be beneficial if the neuralgic pains are severe at the onset. It may be prescribed in suspension in water, or in cachets. For headache, phenacetin (10 gr.) given every four hours is a reliable remedy, but it should not be administered over long periods.

Phenazone in similar doses is equally efficacious but slightly more depressing. Lactophen (10 gr.) and Salipyrin (20 gr.) are also useful. Pyramidon (Di-methyl-amido-phenazone) (3 gr.) is a remarkable antipyretic, but sometimes causes unpleasant collapse even in small single doses. The urea derivatives, Veronal (Di-ethyl-malonyl-urea, or Barbitone B.P.) (5 gr.), Adalin (Bromo-diethyl-acetyl urea) (5 gr.), and Bromural (α-Brom-iso-valerianyl urea) (5 gr.), given in single doses (not to be repeated) act as sedatives, relieve headache and procure sleep; but this group is dangerously toxic.

Dover's powder (10 gr.) is a very good remedy to employ at the first onset of influenza; it relieves the general malaise and the headache, and usually secures refreshing sleep.

Diet.—At first there is usually complete anorexia. The patient may feel disinclined for even milk and soda-water; clear soups, broths

and meat extracts are more palatable and refreshing. Fruit, especially oranges, grapes and limes, are pleasant, and leave the mouth clean. Lemon drinks, barley and oatmeal gruel, especially when iced, often meet with approval. Farinaceous and starchy foods are not as a rule well digested; milk and milk puddings may be nauseous. The best way of giving milk is in the form of junket or whey, particularly the white-wine whey made with sherry instead of rennet. Eggs are not appreciated in any form in the early stages except under the guise of albumen water. An occasional egg-flip with brandy can sometimes be tolerated.

With the gradual return of the appetite fish and meat without vegetables may soon be given. They are generally preferred plainly cooked; a little boiled sole and a grilled mutton chop or cutlet without fat seem to find favour. A small slice of not over-cooked roast beef or mutton is sometimes eaten with relish. As the appetite is restored alcohol may with advantage be added to the diet; not in the grudging shape of an indifferent wine disguised by medication, but the best the cellar can provide : a warrantable champagne, a burgundy full bodied and well flavoured, or a port of known vintage. Thus, by appealing to the mind and the eye, the palate may be tempted to viands for which it feels little inclination.

Influenza frequently presents symptoms of a definitely localised nature and assumes one of four well-recognised types, namely, respiratory, nervous, gastro-intestinal and cardiac.

1. **Respiratory Type.**—In this form the brunt of the disease may fall upon any portion of the respiratory tract, from the nasal passages and accessory sinuses to the lungs and pleura. In addition to drugs intended to counteract the general effects, local treatment of appropriate kind is indicated. It is unnecessary to go too closely in this chapter into details of treatment of the rhinitis, laryngitis, bronchitis, bronchopneumonia and pleurisy of influenza. The treatment does not differ essentially from that proper to these complaints when due to other causes. The irritable cough of influenza without actual bronchitis is often very wearying to the patient, and may assume a spasmodic form resembling whooping cough. Heroin (Di-acetylmorphine or Diamorphine B.P.) is a valuable sedative for this cough, and may be given in the form of a syrup—

Heroin Hydrochloridi gr. $\frac{1}{16}$
Acidi Phosphorici Concentrati ♏ ss
Syrupi ℥ i

or in any of the excellent acetomorphine preparations. Glycerinum acetomorphinæ (= $\frac{1}{36}$ gr. in 1 dr. approx.), Elixir Acetomorphinæ et Terpini (= $\frac{1}{18}$ gr. and $\frac{5}{9}$ gr. of each in 1 dr.), or one of the following pastilles: Pastillus Acetomorphinæ ($\frac{1}{20}$ gr.); Pastillus Acetomorphinæ Comp. ($\frac{1}{32}$ gr.); P. Pini et Terpini et Acetomorphinæ ($\frac{1}{48}$ gr.); P. Terpini et Acetomorphinæ et Menthol ($\frac{1}{400}$ or $\frac{1}{100}$ gr. of Acetomorphine).

A linctus containing opium is useful, such as Gee's linctus (Tinct. Camphoræ Co., Oxymel Scillæ, Syrup Tolutani, equal parts, dose 1 dr. = Opium $\frac{1}{12}$ gr.). Steam inhalations with Eucalyptus, Tinct. Benzoin Co., or Ol. Pini Sylvestris, sometimes give great relief. If the cough assumes the spasmodic form, an adult may learn to control and stop it completely by voluntary effort.

The respiratory complications of influenza should never be made light of. Bronchitis, bronchopneumonia and pleurisy, however slight they at first appear, may prove both dangerous and long lasting. From the nasal mucosa the infection may spread to the accessory sinuses; a complication which should always be suspected and looked for by transillumination or exploratory puncture when persistent facial or frontal neuralgia is complained of.

2. **Nervous Type.** There is a multiplicity of forms included in this type. A rough grouping is possible into a class characterised by pain, myalgia and neuralgia, a class in which psychoses predominate and influenzal meningitis. Myalgia and neuralgia may be relieved by local application of heat, counter irritation, or anodyne liniments such as Linimentum or Glycerinum Belladonnæ, Lin. Aconiti, Belladonnæ et Chloroformi, or methyl salicylate. Occasionally the neuralgia may persist for months after the acute attack has passed. Fresh air, exercise and a generous diet are more valuable in such cases than drugs. It is in these cases that special caution should be exercised against the formation of a drug habit. Temporary cessation of the pain can be obtained by using morphia, opium, heroin, acetanilide, phenacetin, either with or without caffeine, phenazone, and many other well-known drugs, all of which should be avoided whenever possible. The psychoses must be treated as necessity dictates; but fresh air and gentle exercise without fatigue are the first essentials of the cure. It is most important that return to brain-work or the strain of business life should be forbidden whilst any sign of mental unbalance remains.

Meningitis.—Reports of the efficacy of vaccine therapy in the treatment of influenza have recently been published in many journals, and it certainly seems as though this line of treatment should be promptly adopted when the diagnosis can be established.

3. **Gastro-intestinal Type.**—Rest, warmth and starvation may be said to sum up the treatment of acute gastro-intestinal cases. The patients

may be able to take plain water and should do so if possible. Stimulants may be necessary if there is profound collapse. In the less-dangerous cases an initial dose of castor oil (½ oz.) with tincture of opium (15 min.) should be followed by a bismuth mixture to which may be added small doses of opium (Tinct. Opii, Pulv. Cretæ Aromat. Opio, Pulv. Kino Co. or Tinct. Chloroformi et Morphinæ Co.). Bismuth B-Naphtholate (20 gr.) is a particularly good preparation to use in the gastro-intestinal type of influenza. But constipation must be avoided.

Recovery is sometimes extraordinarily rapid, and after living for a day or two on water and peptonised milk the patient may demand a good dinner: and no ill-effects follow if the request is granted. In fact it may be made a general rule to feed up the patient as early as possible in any form of influenza.

If the tongue remains coated with fur, small doses of calomel and saline aperients are beneficial. Stimulants are sometimes necessary in this form of influenza; alcohol may be given with good effect.

4. **Cardiac Type.**—The cardiac enfeeblement produced by influenza is a common symptom which requires serious attention. It may either occur during the height of the attack or persist for many months as a grave sequel. Endocarditis, myocarditis or pericarditis may develop, but the most frequent manifestations are of the nature of irregularities in rhythm. Tachycardia, bradycardia or mere feebleness of action producing fainting attacks and palpitations sometimes continue to cause distress and anxiety. The best treatment for any of the cardiac symptoms is rest in bed, followed by the greatest caution in resuming the normal activities of life. Strychnine is most valuable in strengthening the feebly-beating heart, bromides with digitalis often steady any irregularity of action. The patient requires feeding up well, plenty of fresh air even though confined to bed, and the avoidance of worry.

After-Influenza.—The period of convalescence from influenza is so definite a morbid entity as to deserve some title better adapted to its characters than one which, like convalescence, implies a "beginning to be well." In the opinion of many sufferers from influenza the defervescence of the fever and the decline of the acute symptoms only marks the passage from an irksome malaise to a grimmer series of evils.

The prostration and lassitude are disproportionate to the length of time occupied by the actual illness. The convalescent patient nearly always experiences the feeling of "being good for nothing" during a considerable period. Treatment during this stage is difficult and may tax to its utmost the physician's resourcefulness.

The patient must not be allowed to lapse into the idle equanimity of the professional tramp, while at the same time excess of physical or mental exertion must be avoided. Change of climate and scenery, without the fatigue of foreign travel in tourist fashion, may be recommended. Motoring and cycling should not be permitted. Moderate walking or riding can be safely indulged in. The quiet rest that the country or a sheltered seaside village offer is the ideal cure. But this need not entail solitude and boredom. The cheerful companionship of men or books and the pleasures of the table moderately enjoyed will effect more than much physic. Fresh air blows influenza out of the system, and even storm and wet need not keep the patient indoors provided the clothing is suitable and fatigue is not incurred.

Add to this a tonic containing quinine, cinchona or quassia with nux vomica or strychnine, and nothing more may be required. If the appetite does not return and the tongue remains flabby and coated with white fur, a morning dose of Epsom or Carlsbad salts will improve the digestion. Neuralgia, neuritis and neuroses of all sorts following influenza must be treated symptomatically with an ever-present fear of establishing some drug habit.

It is of the utmost importance to bear in mind that those cases of influenza in which complete recovery is long delayed may demand a revision of diagnosis, for some unsuspected complication may be present. Of these, phthisis, nasal sinusitis, otitis media, endocarditis, phlebitis, Bright's disease, diabetes and even locomotor ataxia are the commonest and most likely to be overlooked. Lying previously latent, these may by influenza be insidiously roused to activity and during many months remain undiscovered. Not the least part of the successful treatment of influenza consists in discovering the presence of some other cause of continued ill-health.

Vaccine Therapy.—The practical difficulty which at present stands in the way of treating influenza successfully by means of vaccines consists in the great variety of organisms found in cases diagnosed as influenza. The world-wide pandemics are generally due to *Bacillus Influenzæ* taking on a parasitic rather than a saprophytic rôle; otherwise, the occasions on which *Bacillus Influenzæ* is the infecting agent are comparatively few. Influenzal colds and many limited epidemics are due to numerous other organisms, the chief among them being a *staphylococcus* of one sort or another or members of that group to which the *Micrococcus Catarrhalis* belongs. The attitude to adopt at the present time should invariably be to ascertain first of all the particular bacteria present in the nasal, faucial or bronchial secretions, and to administer, if thought advisable, vaccines in

strict accordance with the bacteriological findings. Neither experience nor reason justifies the administration of some stock "influenza" vaccine to a case designated, on clinical grounds alone, influenza. This is a mischievous form of empiricism which to-day is all too rife.

It cannot be over-emphasised that, in any epidemic, and even in any individual case, the organism may, without varying its identity, so alter as regards its virulence that the vaccines prepared at different times from it display the most extraordinarily diverse properties.

Nevertheless, such good results have been recorded from the vaccine treatment of so-called influenzal meningitis and other cases of infection by organisms giving the characteristic reactions of the influenzal bacillus that, advancing cautiously along this unexplored path, valuable therapeutic progress may be made. J. A. N.

ERYSIPELAS

While it is an advantage if the case can be transferred to a special ward, the usual precautions observed in septic cases are sufficient to prevent dissemination of erysipelas when this is not possible. Special bed-clothing, towels, handkerchiefs and feeding utensils are necessary; the hands of those applying dressings or washing the patients should be covered with sterile gloves, since direct contact is the method by which the disease is likely to be spread.

Care should also be taken to cover the lesion with some form of protective dressing, so as to prevent the patient from infecting other parts of his own body by means of his hands.

The Treatment of the Primary Focus of Infection. It frequently happens that no primary focus of infection can be seen, or that it may have healed before the patient comes under observation. But a careful search must be made for such a focus, which may be within the margins of the buccal or nasal orifices, the vagina or rectum. If a primary focus is discovered, the exudate must be bacteriologically examined. Any open wound should be dealt with by ordinary surgical methods such as the opening of abscesses, the scraping of sinuses, or the extraction of carious teeth.

As it may be necessary later to invoke the aid of an autogenous vaccine, an attempt should be made to isolate the micro-organism responsible, even if no primary focus can be found, although this often results in failure. As a rule the micro-organism cannot be isolated from the bullæ, where it is usually absent, and even if it is seen in films it fails to grow on cultivation. The usual method is to puncture the skin deeply with a needle or scalpel close to the spreading edge of the lesion; cultivations are then made from the serum which exudes, or from rubbings of the raw surface.

General Treatment.—The patient should be put to bed and constitutional treatment begun. Attention to the bowels is of primary importance; small doses of calomel followed within six hours by a full dose of magnesium sulphate or some other saline purge are indicated. If this fails an enema should be given. The diet should be light. In the milder forms of the disease this frequently suffices to allay the constitutional symptoms, which may disappear within twenty-four to forty-eight hours. As soon as the attack has passed off a generous diet should be given, as the high fever so commonly accompanying it is very exhausting. In elderly people especially, stimulants such as champagne and brandy are indicated, even during the attack. Liq. Strych. 3 min., combined with 10 min. of phosphoric acid in an ounce of chloroform water every four hours makes a useful stimulant. Special care is required in cases associated with chronic renal disease, as these are more liable to succumb to the infection; nitro-glycerin ($\frac{1}{200}-\frac{1}{100}$ gr.) has proved to be of service in these circumstances. Certain drugs have been regarded as being specific for the disease, such as Tr. Ferri. Perchlor. (10–30 min.), quinine and sodium salicylate; but the first is of little avail, while the two latter probably act merely as antipyretics.

Local Remedies.—Many local applications have been suggested, but the majority of cases get well without them. However, the affected part should always be protected both from the atmosphere and from possible contact with other parts of the patient's body in order to avoid auto-infection. Covering with sterile lint is all that is required. Starch powder or zinc oxide sprinkled on to this has a cooling and comforting effect. Cooling lotions, such as Lotio Plumbi c̄ Opio, moistening the lint have the additional advantage of keeping the tensely stretched skin softened, and thus relieving pain. A saturated solution of magnesium sulphate has been advocated for its osmotic effect on the swollen tissues. Certain antiseptic preparations may be used with or without previous scarification of the skin over the lesion; carbolised vaseline, ichthyol ointment spread on the lint, or iodex painted over the skin are of the best. A saturated solution of picric acid is advocated by many. Anti-streptococcic or normal horse serum applied locally may meet with success.

Attempts have been made to limit the spread of infection by injecting small quantities of the latter around the edge of the lesion; solution of carbolic acid (1–20) has been similarly used. Fomentations in any form should be avoided.

Certain other methods of treatment are

indicated in the severer forms of the disease. Lymphangitis, lymphadenitis, severe prolonged pyrexia, the isolation of streptococci from the blood stream or metastatic deposits, and the involvement of other organs call for serum or vaccine therapy. While it is true that erysipelas tends to a natural cure, it is wise to be ready with artificial means of inducing immunity.

Serum Therapy.—Mention has already been made of the use of serums as local dressing. For internal administration it is advisable to use the anti-pyogenes (anti-erysipelas) serum, which is prepared by immunising horses with the streptococcus pyogenes or a mixture of different strains of such. The advantage of this over the polyvalent variety depends on the fact that one of the forms of the streptococcus pyogenes is invariably responsible for erysipelas. Large doses should be given in the early stages of the disease. The initial dose should be 50 c.c. given into the subcutaneous tissues, followed by daily doses of 25 c.c. It may also be introduced into the circulatory system mixed with normal saline solution in a similar dose. It is essential that the saline solution should be prepared from freshly distilled water. The effect of the introduction of serum is often instantaneous, the temperature falling to normal within a few hours, and the infection abating at the same time. It must be remembered that in some cases there appears to be no appreciable effect.

Vaccine therapy.—The streptococcus used for the vaccine should if possible be isolated from the lesion; but if this cannot be done, a vaccine should be prepared from a mixture of stock virulent streptococcus pyogenes. A sensitised vaccine may also be used. (See article on *Vaccine and Serum Therapy*.) The dosage depends on the severity of the infection. In the early stages of the disease with marked toxæmic symptoms, but without evidence of bacteriæmia, doses from twenty-five to fifty millions dead streptococci may be given into the subcutaneous tissues, but in the more severe cases smaller doses, starting with one million and rising gradually in daily doses as indicated by the course of the disease should be tried. It is impossible to lay down definite rules as to dosage; broadly speaking it may be said that the more severe the infection the smaller should be the initial dose. Much larger doses of sensitised vaccines may be safely used even in severe cases; with these the intensive method as suggested by Fornet and Muller should be used, *e. g.* doses of ten, twenty-five and fifty millions given on three successive days. The results are variable. In some cases the appropriate dose will cause immediate abatement of the symptoms, with subsequent resolution; if this does not occur with the initial dose, it may follow subsequent inoculations. In other cases each inoculation will cause a marked improvement in the general condition of the patient, without improving the local condition. In yet others no obvious benefit will be obtained.

Treatment of Recurrences.—Recurrences are apt to follow an attack of erysipelas and may be very difficult to deal with. Prophylactic measures are of the first importance. The clothing should be thoroughly disinfected, the patient removed to another room as soon as the infection has abated, and a carbolic bath given. If there is still a primary focus of infection, it should be vigorously treated, then the affected teeth should be removed if there is pyorrhœa alveolaris, any septic condition of the nose should be attended to, chronic ulcers of the skin should be encouraged to heal and sequestra removed from the bottom of sinuses.

If these measures fail to prevent recurrences vaccine-therapy is always worthy of a trial.

Treatment of Associated Symptoms. — Local applications usually suffice to allay pain, but if these fail such drugs as morphine tartrate, $\frac{1}{4}$ gr., may be required hypodermically. Sleeplessness is frequently a troublesome symptom, for which the bromides or aspirin may be used.

Delirium combined with high fever will usually disappear after the use of antipyretic measures. Chloral hydrate is often useful in the more obstinate cases. W. G. B.

PNEUMONIA

The history of the treatment of Lobar Pneumonia before the time of Louis and Skoda is an unprofitable study save in so far as it serves to illustrate the Hippocratic maxim that experience is fallacious. Sir Thomas Watson little dreamt how posterity would come to judge his warning words when he wrote, "Very lately one most distinguished French writer, M. Louis, has endeavoured to show that venæsection has not much control over the progress or event of pneumonia; and I advert to his opinion on this subject merely to caution you against being misled by it; as you might otherwise be considering his well-merited reputation as an exact and faithful observer." The active plan of antiphlogistic treatment of pneumonia by copious bloodletting, mercury and tartar emetic has given place to the expectant method, and the modern therapy consists in endeavouring to maintain the patient's strength whilst the disease runs its course, which fortunately is as a rule short. In spite of much searching after a specific remedy wherewith to counteract directly the activity of the pneumococcus or minimise the effects of its toxines no reliable

cure for the disease has yet been discovered. The treatment resolves itself into two parts—general and symptomatic.

General

At the outset the surroundings and nursing of the patient demand attention. A large, airy and well-lighted room is necessary, where the patient may be kept in bed. The bed should not be too wide, nor the mattress too soft. The bed-clothes should be warm enough without being heavy, and in cold weather it is better to rely upon hot bottles rather than extra bed-clothes. A light flannel jacket or a so-called "pneumonia jacket" made of gamgee tissue is useful, as it enables the patient to be propped up in a sitting position without regard to covering the upper part of the body with bed-clothes. This is also convenient for the physician's examination of the chest. Adequate skilled nursing is of the utmost importance, and the use of the bed-pan is imperative. The number of persons in the room must be limited to one or two, conversation restricted and the patient allowed to talk as little as possible. Tepid sponging of the whole body once or twice a day is as a rule comforting even if the fever is not high. The mouth and nose should be kept carefully cleansed and the skin of the back tended with the usual precautions. The patient, if unable to move, should not be permitted to remain in one position too long at a time, nor allowed to slip down too low in the bed.

Diet.—The diet should be light and nutritious. Digestion is always impaired during the acute stages of the disease. Plain water, lemonade or lemon drinks should be given freely. Milk, either plain or with soda-water, peptonised milk, junket, whey and eggs either raw or lightly boiled, are the most suitable food. The addition of carbohydrates to the food in the form of cane- or milk-sugar should not be forgotten. Beef-tea, soups, broths and meat jellies or extracts are useful as stimulants, but they have no great nutritive value. Small quantities of prepared protein food powder may be added to the milk with advantage. The foods prepared from one of the cereals are useful by way of change and their digestion may be aided by the administration of taka-diastase or pancreatin.

Drugs.—No drug exercises any direct influence on the course of the disease. In the initial stages a mild diaphoretic mixture containing liquor ammoniæ acetatis may promote a sense of comfort and does no harm. Expectorants are useless and worry the patient. Free water-drinking increases the flow of urine and may assist in the elimination of toxines. At the onset it is well to open the bowels freely with calomel or blue pill followed by a saline. Afterwards drastic aperients should not be given, mild salines or simple enemata are preferable. Tympanites is a distressing and, in children, common symptom, due in part no doubt to the limited diaphragmatic movement, and in part to the constipation which accompanies the fever. Constipation may be avoided by water-drinking, but if distension occurs turpentine enemata or the use of a rectal tube will generally give relief. In pituitary extract we possess a most reliable remedy for tympanites.

Symptomatic Treatment

Pain.—The intense pain in the side at the onset of the disease may be relieved by linseed or linseed-and-mustard poultices, especially in children. The poultice should be applied to the side or base of the lung affected and should not encircle the whole chest so as to impede the already embarrassed movements of respiration. The poultice should be taken off before it gets cold and clammy, the skin should be dried and a pad of warm dry wool placed round the chest. Leeches (six to twelve) applied over the site of the pain or pleural friction may prove of great service. The continuous application of an ice-bag is a not unpleasant alternative, but it is sometimes difficult to keep it in contact with the chest without uncomfortably firm bandaging. A mustard leaf or blister is also useful. For the severest forms of pain a hypodermic injection of morphia ($\frac{1}{4}$ gr.) may be necessary. Dover's powder often gives very great relief in the initial stages of pneumonia where there is much pain, and is suitable for administration to children no less than to adults.

Toxæmia.—When the initial toxæmia is severe and the shock of the invasion profound, as often occurs in children, stimulants are necessary. Brandy, spirit of ether, Hoffman's anodyne, or sal volatile may be given by mouth, or hypodermic injections of strychnine or camphor (5 min. of a 10 per cent. solution of the latter in olive oil for children). During the later stages of the disease when the fever is at its height the toxæmia bears apparently little relation to the extent of the physical signs of pulmonary consolidation. Although this indication of the progress of the disease is one which the physician watches with the utmost care and maps out with geographical precision, it must nevertheless be admitted that the treatment is rarely influenced by the information so gained. This is true at least so long as the signs remain only indicative of solidification of the lung, no matter over how large an area. The prognosis may be influenced, but not the therapeutics of the case. On the one hand recovery may take

place in spite of the most extensive involvement of the lungs, whilst on the other hand heart failure often occurs with quite limited consolidation. The treatment of toxæmia consists in *hydrotherapy*, free water-drinking to flush the kidneys and avoid constipation, in sponging the whole body frequently with either hot, tepid or cold water, according to the preference of the individual patient or in water compresses (60° F.) to the chest. Stimulants, as described previously, may also be required when the toxæmia is profound.

The Heart.—It is a mistake to exhaust our battery of drugs in the routine stimulation of the heart in every case of pneumonia. Many patients will, if left wisely alone, make good recoveries. In determining whether stimulants are necessary, the guiding rule should be that "anything which weakens the heart weakens the first sound." The first heart sound must be diligently observed, since from its quality much information may be gained. In a failing heart the systolic and diastolic intervals tend to become equalised. Some degree of cardiac dilatation need not occasion alarm, it is perhaps an inevitable consequence of, and compensation for, the respiratory embarrassment. Digitalis is undoubtedly a useful drug, and the freshly made galenical preparations are better than the much-advertised proprietary derivatives. Ten minims of the (standardised) tincture may be given four-hourly. Ether, nux vomica and brandy are also useful. The latter is especially so in old persons and those accustomed to take it habitually. Hypodermic injections of strychnine (5–10 min. of the Injectio Strychnin. hypod. B.P. 1914) may be given. Injections of camphor (5–20 min. of a 20 per cent. solution in olive oil) provide one of the most valuable stimulants in pneumonia. Care must be taken to inject camphor into the deep tissues and not immediately under the skin. Camphor injections may be given frequently and over long periods. It is a good plan in severe cases of heart failure to employ alternately camphor and strychnine injections every two hours. Caffeine (5 gr.) acts well in pneumonia, and its effect is increased by administration in strong coffee. Ammonium carbonate (3–10 gr.) is an excellent cardiac tonic, which is least unpleasantly prescribed in milk; but unless the patient has already begun to expectorate, it may increase an ineffective and painful cough in a troublesome way. Although tincture of musk has gone out of fashion, there are some patients who respond to its administration in drachm doses quite surprisingly. If dilatation of the right side of the heart supervenes with great cyanosis, venesection (15–20 oz.) should be performed. Children and thin, ill-nourished adults tolerate bloodletting extremely badly and are rarely benefited thereby. Inhalation of oxygen sometimes produces good results, but on the whole the great expectations formed of this remedy have not been realised, except in children, who, for some reason, usually respond well to oxygen.

Pyrexia.—A certain degree of fever is part and parcel of pneumonia; it is not an unfavourable sign and no active measures need be adopted for reducing it. Apyretic pneumonia bodes ill for the patient. Antipyretic drugs, such as antipyrin, phenacetin, acetanilide, pyramidon and the like, do no good and are powerful cardiac depressants. If the fever is of such a height as to make the patient restless and sleepless, sponging with hot, tepid or cold water is the safest and best means to adopt for reducing the temperature. Ice-cradling is excellent, it does not disturb the patient and rarely fails to promote a feeling of comfort, allay restlessness and ensure sleep. The simple process of reducing the bed-clothes to a single sheet is often forgotten; patients with fever do not catch cold. An ice-bag continuously applied to the head with hot bottles about the feet and legs will often soothe a restless patient.

Delirium.—Great danger is to be apprehended from violent delirium, chiefly because of the physical exhaustion it entails. Experience shows that there are two types of delirium met with in pneumonia, alcoholic and toxæmic or pneumonic. Of these the first is by far the less dangerous. In alcoholic delirium, at any rate, mechanical restraint of the patient's movements by a sufficient number of skilful attendants is the best method of control. In either type of delirium, sedative drugs, although they may be necessary, are never harmless. Hyoscine ($\frac{1}{200}$–$\frac{1}{50}$ gr.), given hypodermically is the least harmful. Bromide of potassium and chloral are not safe; they increase cyanosis and profoundly depress the heart. Morphia does not deserve all the hard things that have been said of it. Provided the kidneys are excreting sufficient urea, and provided there is no great degree of cyanosis, a hypodermic injection of morphia ($\frac{1}{4}$ gr.) combined with strychnine ($\frac{1}{100}$ gr.) may be advantageously employed in the treatment of delirium. Dover's powder (10 gr.) is the best and safest preparation of opium to use in the milder types of pneumonic delirium.

Insomnia.—Sleeplessness without delirium is not common in pneumonia; if it should occur, paraldehyde (1 dr. in 1 oz. of Mist. Amygdalæ) is a remedy worth trying. Its drawback lies in its capricious action. It acts as an hypnotic in disappointingly few cases, but when it does act it is preferable to any other drug. Hyoscine, opium and morphia may be used with caution. The objections to bromide and chloral have been mentioned under the treatment of delirium.

Sulphonal, trional, tetronal and above all veronal are unreliable and dangerous. Sponging and ice-cradling will often promote sleep. Oxygen frequently acts like a charm in children, but a good nurse will get a child to sleep where drugs are of no avail.

Cough.—In the early stages of pneumonia the cough is distressing and unprofitable. It may be diminished and relieved by poulticing the chest, by the application of an icebag to the affected side, or by strapping the side. Simple demulcents may be given, or, if the cough is excessive and exhausting, Dover's powder, opium, morphia, codein or heroin (Heroin Hydrochloride Diamorphine hydrochloride B.P.) may prove useful. The early cough is due to pleurisy and there is no reason why it should not be checked. But in the later stages, when resolution has begun and there is some sputum to be expectorated, the cough is useful and should not be stopped unless it appears to be in excess of the patient's needs. When bronchitis is present the cough does good rather than harm. In these circumstances the cough should be assisted by expectorants. If the sputum is thick, tenacious and got rid of with difficulty, ammonium chloride or carbonate (3 gr.), guaiacol (1–5 min.), creosote (1–5 min.) and terpene hydrate (2–6 gr.), help to make the secretion more easily expectorated. Small doses of Vinum ipecacuanhæ (10 min.) or Vinum Antimoniale (10 min.) occasionally do good, as also does potassium iodide (5 gr.) in cases where the patient is able to cough but cannot dislodge the mucus; but these three latter remedies should not be given frequently, nor over periods of several days. They impair the appetite and digestion and depress the heart. Strychnine or nux vomica will often relieve the patient by enabling a stronger cough to perform with less effort the task of clearing the lungs of secretion. Steam-tents and bronchitis kettles scarcely ever do good in pneumonia, and an atmosphere heavily laden with moisture adds to the patient's respiratory difficulties.

Complications

Not the least important part of the treatment of pneumonia lies in the early recognition of certain complications.

Empyema is the complication whose early discovery is of the greatest moment to the patient. Unresolved pneumonia may occasionally exist, but it is a diagnosis with which no physician should rest content until established by necropsy. Most cases of unresolved pneumonia so diagnosed during life turn out to be cases of empyema. The assistance of the X-rays should always be sought to supplement the exploring syringe in cases suspected of being empyema or diagnosed as unresolved pneumonia. Early exploration on very equivocal physical signs is not only justifiable but imperative. Repeated explorations should follow a negative result; if the patient's condition and physical signs justify the suspicion of empyema a single negative exploration does not suffice to establish a contrary conclusion that pus is not present somewhere in the chest. Apical and interlobar empyemas are always puzzling, and a protracted case of pneumonia in a child is generally due to empyema, even though the physical signs do not suggest its presence. All cases of empyema should be treated by an early operation with resection of portions of one or more ribs and free drainage.

Serous effusion requiring aspiration hardly ever complicates pneumonia. The presence of a large serous effusion should always rouse a suspicion that the case is tuberculous in origin.

Gangrene of the lung is not invariably fatal; inhalations of creosote, guaiacol or turpentine may relieve the condition if the gangrene is localised and limited to a small area.

Abscess of the lung, if discovered, demands operation and drainage.

Otitis media is a common complication of pneumonia in children and must not be neglected. A discharge from the ear always requires treatment, but if the otitis can be discovered before perforation occurs a timely incision of the membrana tympani will often avert deafness and the many dangers of a chronic suppuration of the middle ear.

Ear-discharges in pneumonia are only too often treated with the light-hearted contempt bred of ignorance. The assistance of an aural surgeon should be sought at the first signs of otorrhœa. Chronic otorrhœa following pneumonia is a reproach to the physician.

Meningitis.—The treatment of pneumococcal meningitis has hitherto not proved encouraging. Possibly vaccine or serum therapy may eventually yield results as gratifying as those of Flexner's serum in cerebro-spinal meningitis.

Pericarditis.—The pericarditis which sometimes complicates pneumonia is unfortunately frequently purulent. Treatment is unsatisfactory and the prognosis bad. The pericardium has been opened and drained for pyo-pericardium. If there is not actually pus in the pericardium the inflammation is generally of a plastic type and may involve the mediastinum.

Endocarditis is a complication which if recognised can only be treated as in rheumatic cases, save that salicylates are not indicated.

Peritonitis is a rare complication which if generalised requires immediate laparotomy. The results of early operation are good, those of delayed operation fatally bad. A slighter localised peritonitis limited to the under surface of the diaphragm will probably escape recog-

nition, and so long as it remains localised does little harm. It will, in the majority of cases, be regarded as a localised pleurisy and receive equally appropriate treatment.

Arthritis.—A red, painful, swollen joint occurring in the course of, or during the convalescence from, an attack of pneumonia should be explored early with due attention to asepsis. Joints infected by the pneumococcus usually suppurate. They should be freely opened and drained if pus is discovered. A sound movable joint should result from the early diagnosis, and drainage of a suppurative pneumococcal arthritis.

Other rarer complications such as **phlebitis, nephritis** and **peripheral neuritis** do not differ in their therapeutic requirements from the same conditions excited by other causes.

Many of the complications of pneumonia are suppurative and require surgical operations. There is sometimes a tendency to hesitate to advise operation because of the desperate condition of the patient. No patient suffering from pneumonia should ever be regarded as too ill to have pus evacuated. In pneumonia an operation is borne well even if a general anæsthetic is contra-indicated. Under local anæsthesia operations of considerable magnitude can be performed. It is a mistake to delay a necessary operation until the patient is convalescent, the patient will probably not convalesce so long as he is harbouring pus.

Convalescence and After-Care

In an uncomplicated case where resolution proceeds normally the patient may be allowed to get up a week after the crisis. If the pulse becomes unduly rapid with exertion and movements, caution must be used; a simple measure of the heart's recovery of tone lies in the length of time taken by the pulse to regain its previous rate after being quickened by sitting up in bed. In a healthy convalescent the pulse-rate should steady down in two or three minutes at most. A low blood pressure (90 min. Hg. or less in an adult), indicates lack of tone in the heart-muscle. Rest, fresh air and tonics are the only remedies needed, plenty of good food is more important than anything else.

The after-care of pneumonia should entail as long a rest from work as possible with change of air to a mild, warm, dry climate. Whether pneumonia predisposes to phthisis or tuberculous subjects are unduly liable to pneumococcic infections, the fact should be realised that a large proportion of phthisical patients give a previous history of one or more attacks of lobar pneumonia.

Children appear particularly liable to repeated attacks of pneumonia; considerable care should be exercised with a child for some years after a first attack.

Specific Treatment

Although up to the present no great progress has been made in treating pneumonia either with vaccines or antitoxic sera, there is no reason to adopt a hostile attitude to remedies of this nature. Sometimes it has seemed that if administered in the earliest stages anti-pneumococcus serum has exercised a modifying influence upon the subsequent course of the disease. But this is a matter very difficult to judge, pneumonias vary so much in their effect upon individuals and in their own "epidemic constitutions." Vaccines prepared from the pneumococcus have so far failed to justify their use in general pneumococcic infections such as pneumonia, but in chronic local suppurations good effects have been reported.

The time is not yet ripe for expressing an opinion upon the possibilities of treating pneumonia by intravenous injection of bactericidal drugs. In ethyl-hydro-cuprein-hydrochlorate Morgenroth claims to have found a chemical agent which exerts its destroying effect upon the pneumococcus practically undiminished in serum. This drug administered intravenously has been found capable of curing pneumococcus septicæmia in mice, and provides, as Sir Almroth Wright has said, "the first demonstration of the possibility of preventing and curing a bacterial—as distinguished from a protozoal or spirochætal—infection by the administration of a drug." In the few human subjects to whom Morgenroth's drug has been administered its effects have proved it to be dangerously toxic and optico-neurotropic, while at the same time it has failed to affect the course of pneumonia. Wright suggests as an explanation that the consolidated lung offers a nidus to bacteria where they are safe from the deleterious effects of a drug in the blood-circulation that cannot penetrate to them. Hence the success in mice where the injection is septicæmic and the failure in human pneumonia where the drug has only restricted access to the infecting microbes. J. A. N.

UNDULANT OR MEDITERRANEAN FEVER

Distribution.—This disease is most common around the shores of the Mediterranean, but has lately extended into European countries (Portugal, Spain and France). Other endemic areas are present in India, China, North and South Africa, America, and Peru; in fact, the disease has now become world-wide.

Etiology.—It attacks all ages and both sexes, but generally has the highest incidence in women and young adults, occurring in all seasons, but particularly in the hot dry weather. The disease was frequently found in association

with typhoid in the Mediterranean, a person recovering from the former suffered often from a prolonged fever due to the latter infection.

The cause of the disease is the minute coccus, the *M. melitensis*, which produces an acute or chronic septicæmic condition. The organism may gain access to the body (1) by food, particularly in milk; (2) occasionally by infection through the skin and mucous membrane. Wherever goat's milk is a staple diet the disease tends to be endemic—goats being commonly affected though rarely showing any evidence of the disease. Cows also may be infected, and their milk can convey the dangerous organism. The infection is conveyed from man and animals chiefly by the urine, fæces and milk.

Symptomatology.—The disease may commence as an acute fever simulating typhoid and malaria, or it may run a subacute or chronic course, producing intense cachexia with anæmia and persistent neuritis. During the febrile state rheumatic-like symptoms may be present with some gastro-intestinal disturbance, excessive sweats, constipation, endocarditis, orchitis, lobular pneumonia or pulmonary œdema; nephritis and hæmorrhages are rare. The course of the disease extends on an average over three months, but it may be prolonged to two years. The nervous symptoms are generally marked : at first there are insomnia and slight delirium, then great depression and a tendency to nerve pains, such as sciatica and neuralgia, sometimes giving rise to a local paresis of groups of muscles. Cardio-vascular symptoms are common : irregular palpitations from slight mental or physical causes, rapidity of pulse with irregularity of force, volume and frequency. The changes in the blood are important; there is generally a reduction in the number of red cells and a low colour index—a marked reduction in the polynuclear cells and a relatively marked increase in the mononuclears giving rise to a general lowering of resistance to bacterial infections. Death may be brought about by hyperpyrexia, heart failure, and pulmonary complications.

The diagnosis may be made by the clinical symptoms : the long fever with rheumatic-like pains, sweats, constipation and cachexia, but most accurately by culture of the organism from the blood, or by agglutination reactions, which are present early and are given with high dilutions of the serum. The latter are specific in character if certain precautions are taken.

Occasionally the organism may be isolated from the urine, and the diagnosis confirmed thereby.

Prophylaxis.—As the exciting cause in the great majority of the cases is the entrance into the body of the micro-organism by milk, it is essential that in the endemic area this shall be rendered free from infection. In the Mediterranean and parts of South Africa, etc., goat's milk is almost universally used, and as this is now known to be so frequently infected, sterilisation must be effectively carried out. This can be done by boiling the milk, and that this has been effectively done can be ascertained by using the Ortol test. It must be remembered also that not only goat's milk, but cow's milk may be dangerous, and that the products of milk, such as cream, butter and cheese may convey infection; some cases have even been traced to ice-cream in Algeria. Infection in infants is conveyed by the mother's milk (Italy).

Treatment of the Disease.—Disinfection of all infected material from the patient must be carried out as in typhoid. In all cases of undulant fever it is important to remember that we are dealing with a specific disease over which we have no certain control and that it tends to run a very long course. It is of the very first importance so to conduct the treatment that the patient's strength shall be maintained by giving as much food as he can assimilate; we must also counteract the secondary anæmia, and symptoms must be relieved by appropriate measures. We may also attack the cause of the disease by means of vaccines.

With such a long and tedious disease good nursing is of great importance. In an acute case a comfortable bed in a well-ventilated room, which can be kept at an equable temperature with cheerful surroundings, is required.

A trained nurse is almost always necessary, for at first the course of the disease may be as severe as in a bad case of typhoid fever, giving rise to high pyrexia, gastric discomfort, slight delirium, insomnia, sweats and other symptoms of a severe toxæmia; here, then, a good nurse or nurses are required to carry out measures to keep down the fever, regulate the food, and attend to the comfort of the patient. The danger line of fever is often put at 103°, when tepid sponging is necessary; if the temperature rises to 104°, cold sponging; and above that a wet pack may be required. Great attention should be paid to the pulse and the condition of the skin; if the former is weak a stimulant should always be combined with the antipyretic measure; great care must be taken never to check sweats, if present, by hydrotherapy. A continued type of fever lasting three to four weeks, if uncontrolled, produces a marked effect upon the cardiac and nervous system, so that tachycardia and persistent neuritis appear. Constipation generally is a marked and early feature; as soon as the diagnosis has been made, small doses of calomel, saline purges, or better still, cascara and enemata, may be used. Sweats are frequently very severe and distressing, either

local or general; as in rheumatic fever, the patient should be kept between blankets and the skin frequently dried and powdered; this will materially decrease the discomfort. If rheumatic symptoms affecting the joints appear, as they are apt to do, hot opium fomentations, or belladonna liniment associated with perfect rest, gives the most relief. One of the most distressing symptoms in acute cases is the persistent insomnia. The patient should *never be allowed to pass sleepless nights.* Trional, sulphonal or other mild hypnotic preparations should be given. At first, the patient should be kept upon a restricted typhoid diet until the diagnosis is assured, when light soups, eggs, custard puddings, Benger's food and sanatogen may be given, always using the condition of the tongue as the main guide. If the tongue is fairly clean, the fever moderate, and the assimilation good, a very low diet is contra-indicated. Stimulants are not required, and should not be given at first; in the third, fourth or fifth week they will probably be most useful, and should be reserved to help a flagging heart enfeebled by continued pyrexia.

As to drugs, quinine is useless in large doses, but I have found that combined with chlorine (Burney Yeo's mixture) it did in some cases apparently shorten the pyrexia attacks; Hartigan recommends cyllin—but no drug has any specific effect. Digitalis, strychnine and ammonia may each render assistance in acute conditions when the toxæmia is most severe. Abundant cooling drinks are most gratifying; when the mouth and tongue are dry and foul, sulphurous acid as a wash is very beneficial, generally more so than boracic acid and myrrh, carbolic acid or listerine.

Both the condition of the lungs and kidneys should be watched from day to day. Anti-pyretics like phenacetin and antipyrin are generally to be avoided.

After the primary wave has passed off, each recurring attack of pyrexia increases the anæmia, the tendency to neuritis and the general cachexia; the patient loses weight steadily, becoming more and more depressed, and is liable to orchitis, boils, etc. The careful feeding becomes more and more important, and efforts should be made to combat the anæmia by mild iron preparations such as dialysed iron, Blaud's pills, etc., and ferro-glidine given with milk or with strychnine. Diffusible stimulants, such as brandy and champagne, will be helpful now. Later, when a low, hectic type of fever comes on, as in the third month and after, arsenic and iron are called for either by the mouth or by intra-muscular injections, and I have found preparations of yeast useful not only in increasing the number of white blood-cells, but also in reducing the tendency to neuritis; two drachms of fresh yeast may be given twice a day on bread and butter as a sandwich, or in milk; capsules of nucleic acid are also useful. In the chronic stages, massage of the wasted muscles should be used daily, and for the chronic neuritis high-frequency treatment is sometimes very beneficial. If pain is persistent, a liniment of aconite, belladonna, or camphor gives relief. In convalescence some malt alcoholic drinks may be given with food, such as good stout and porter, or port wine if preferred.

During convalescence warm clothing, fresh air and sunshine, with gentle exercise, must be insisted on, and frequently a change of surroundings brings about a cure when other means have failed; but the patient must be warned that a chill or over-exertion is liable to induce a relapse. Serum therapy has not given satisfactory results. A nucleo-proteid serum has been prepared by Donzello-Trambusti and is said to be effective, but much more evidence is required. Vaccines made of dead emulsions of the *M. melitensis* have been fairly tried. From a large series of cases in Haslar hospital and elsewhere I have found that their use was of no advantage in the acute stages of the disease, but during the chronic toxæmia with a low, irregular fever they appeared to cut short the disease. Their administration is scientifically justifiable and reasonable, for we know that the organism can remain alive for long periods in the spleen and other organs; therefore any measures are called for which increase the phagocytic activity of the cells in the blood tending to destroy the infecting agent. The two most important means to this end are appropriate vaccine therapy and the administration of yeast or nucleic acid. Scardo (Francesco) from experiments carried out at Rome on goats artificially infected with *M. melitensis*, obtained some good results with intravenous injections of corrosive sublimate (using Bacelli's formula). This method he is now going to apply to human cases with great hope of cutting short the fever.

A micrococcus paramelitensis has lately been described which is probably the cause of several anomalous forms of fever in the endemic area in which the ordinary serum diagnostic test has failed, and for which a special vaccine would be required. P. W. B.-S

POLIO-ENCEPHALO-MYELITIS, "POLIOMYELITIS"

Poliomyelitis and encephalitis is an acute specific fever communicable from individual to individual and must be treated as such. Unlike the other acute fevers, however, which for the most part rapidly clear up and leave no sequelæ, poliomyelitis, owing to damage done to the

nervous system during the acute stage, commonly leaves a residual paralysis of a variable degree.

The organism by which the infection is carried belongs to the group of "filterable viruses." It is present in the nasal and pharyngeal mucous membrane, and may remain in this situation for at least six months after the onset of the disease. It is present in the blood during the prodromal stage of the disease, and may experimentally be communicated from animal to animal by means of biting flies. It is also present in the intestinal mucus. The incubation period of the disease is experimentally eight to twelve days, but clinical evidence points to a shorter period, probably about four days. The infection may be carried by a third person.

General Treatment.—A case of acute poliomyelitis should be treated in regard to infection like a case of typhoid. In hospital "bed isolation" should be insisted on: in a house "room isolation." Swabs used for absorbing nasal and buccal secretion should be burnt and fæces and urine mixed with a disinfectant before being discharged down the drain. Bed-linen, articles of apparel and all utensils for food should be treated in the same manner as for a typhoid patient. In summer the risk of fly infection should be prevented by the use of a "mosquito net." Since the incubation period varies from eight to twelve days a *quarantine period* of at least *fourteen days* should be given to all contacts.

The *period of isolation* of the person infected should be at least twenty-one days, and he should be free from all nasal, ear or other discharge. The nasal and pharyngeal cavities should be syringed out with a solution of chlorine water or potassium permanganate 0·2 per cent. for a week before the termination of the period of isolation. There is evidence that "carriers" may occur, but the method of determining such is at present too difficult and uncertain to be of practical service, and since the infectivity of the disease is considerably less than diphtheria, the risk run is very slight if the above precautions are taken.

Treatment of the Acute Stage.—During the early stage of the disease *pain* is the symptom which demands the greatest attention. It is the symptom which renders these cases liable to be mistaken for rheumatism.

Absolute rest and freedom from jars is essential, and this is best secured by placing the patient on a water bed, the limbs being carefully supported in whatever position is most restful. Acetyl-salicylic acid, or salicin in 3–5 gr. doses every four hours will often help to allay the pain, but in some of the severest cases pain is only relieved by morphia. This drug needs, however, to be used with the greatest caution, and in small doses if the respiratory muscles are affected, and when given in such cases should be combined with $\frac{1}{200}$ gr. of atropine.

It is advisable to give 5–10 gr. of hexamethylenetetramine (urotropine) during the acute, and if possible during the prodromal, stage of the disease, for it has been shown experimentally that this drug passes into the cerebrospinal fluid and delays, if it does not always inhibit, the experimental infection of animals. It can safely be given in the above doses to quite young children.

Lumbar Puncture should always be performed during the acute stage, not only for diagnostic purposes, but also for the relief of pain. The cerebro-spinal fluid is always under increased pressure, and in many cases relief of pain is afforded by this means. Clark has shown experimentally that the injection of 1·5 c.c. of 1 in 1000 solution of epinephrin has a marked effect in limiting the spread of the disease, and this method of treatment might well be used in severe and ascending forms of poliomyelitis.

When the disease is of wide extent and the muscles of respiration and deglutition are affected, great care must be exercised in feeding the patient. If there is any evidence of failure of the glottis to close whilst the patient is being fed, it is advisable to feed the patient with a tube passed into the stomach.

After the acutest stage of the disease is past, which usually lasts from five to ten days, recovery begins to take place. The temperature becomes normal, pain ceases and the extent of the paralysis can be accurately determined. It is, however, most essential at this stage to keep the child at *absolute rest* for at least a month from the onset of the disease; for unless this is done there is a risk of the disease extending.

The important points in regard to treatment at this stage are the *prevention of contraction and deformities, the maintenance of the temperature of the limbs, and the stimulation of the muscles* so as to keep them in a good condition whilst the damaged neurons are recovering.

Contraction of muscles which produces deformity is best prevented by massage, passive and resistance movements and by the application of a *light splint* which will keep the leg in a normal position. *A "celluloid" splint* carefully moulded to the leg is most suitable for this purpose and should be worn both during the day and night.

Massage, active and passive movements, may be begun in the third or fourth week after the onset of the disease, and should be given twice a day for half an hour at a time.

The application of electricity in its various

forms is of considerable value, but it is important to use that form of current to which the paralysed muscles respond. The question as to the length of time for which the treatment by massage and electricity should be carried out is one which can only be decided in each individual case. In all severe cases it should be carried out for at least two years.

Warmth is most essential for the good recovery of the limbs affected, and this should be maintained by loose woollen stockings and overalls, friction to the skin, and by the application of heat.

In the later stages of the disease some *mechanical support* is often required in order to help the patient to walk, and also to prevent the occurrence of deformity. A well-fitted "celluloid" splint is probably the most convenient form, for it is light, it can be worn both during the day and night, and it keeps the affected muscles in a position of rest and thereby tends to hasten recovery.

In the second year after the onset of the disease a splint with a knee lock and spring attachment to reinforce the weak muscles will for many cases be more convenient. The celluloid splint is, however, by far the most convenient for cases in which there is weakness of the thoracic and back muscles, and also for those cases in which the arm muscles are affected.

Division of Tendons.—In cases in which deformity has arisen it may be necessary to shorten or lengthen tendons, and such treatment in conjunction with other measures is often most useful.

Transplantation of tendons, so-called muscle-grafting, has a limited application, but is of undoubted service in selected cases.

Resection of a joint so as to give a fixed instead of a flaccid joint is of some value in selected cases, but the age of the child, the duration and extent of the paralysis have to be carefully considered.

Nerve Resection and Reunion.—The object of this operation is to connect the proximal end of a degenerated nerve with the distal end of a nerve in connection with healthy nerve centres. The numbers of cases which are suitable for this form of treatment are few, and even those which are apparently suitable have for the most part given most disappointing results. The class of case most suitable is that in which the muscles of the arm supplied by the fifth root are paralysed, whilst those supplied by the sixth root are relatively normal. The operation should be performed before the sixth month after the onset of the disease, but no improvement is to be expected in the condition of the muscles for at least six months after the operation. It should be remembered that although the methods of treatment just mentioned are useful in individual cases the essential treatment lies in the maintenance of the nutrition of the limb by warmth, massage, and active and passive movements.

The line of treatment above described refers primarily to the common form of the disease in which the spinal cord is affected.

The affection of the cerebral hemisphere gives rise to a hemiplegia, the treatment of which should be by massage, and passive and active movements.

In those cases in which the cerebellum is affected ataxia is the leading feature, and this should be treated by a series of movements for re-educating the co-ordination of the limbs by hand and foot-step exercise. F. E. B.

SAPRÆMIA, SEPTICÆMIA AND PYÆMIA

Toxæmia is a general disorder dependent solely upon chemical poisoning of the body. It arises as the result of absorption of the products of bacterial activity, or of metabolic poisons, or of a poison from the alimentary tract. In this section, that form of toxæmia, sometimes termed *Sapræmia*, will alone be considered, in which the intoxication results from the absorption of the products of bacterial activity—their toxins and substances resulting from the disintegration of the tissues in which they thrive. In pure sapræmia, the organisms multiply and remain at the site of invasion and do not gain entrance to the general blood stream. Bacteria will flourish in tissues which are lacerated or bruised, infiltrated with blood or deprived of their blood supply, or injured with chemicals. Thus sapræmia is prone to occur in the puerperium, after burns, large wounds, operations involving the peritoneum, pleura or other serous cavity, and after the removal of tumours leaving ill-drained cavities containing blood and debris.

Septicæmia is that condition in which pathogenic micro-organisms invade the general blood stream and, becoming established, multiply therein. Such septicæmia may be met with—

1. In the course of certain infective fevers, *e. g.* typhoid fever, infective endocarditis, general tuberculosis, plague, as an essential part of the disease.

2. Following a definite local lesion; either primary, as in wound infection, or secondary, where the organism causing the septicæmia is other than that essentially concerned with the initial lesion—as, for example, streptococci in septic scarlet fever or in diphtheria.

3. Arising without any recognisable portal of entry—the so-called cryptogenetic infection.

It is with the two latter group sonly that we are concerned here. When, in the course of

such a general invasion of the blood and tissues, secondary foci of suppuration appear, the condition is called *Pyæmia*. It is seen not infrequently in the puerperium, or in the course of surgical diseases associated with suppuration, such as otitis media, phlebitis, osteomyelitis or bronchiectasis. It occurs occasionally when the external appearance of a wound is satisfactory, though on exploration a septic focus may be found in the depth. Commonly, septic thrombosis takes place in the veins leading from the infected area; the clot softens and portions becoming detached are carried away in the blood stream to lodge in the first capillaries they reach. Thus, where the systemic veins are involved, the lungs are generally the first, and it may be the only, organs in which secondary abscesses develop. Suppuration in the area drained by the portal vein may be followed by portal pyæmia.

The clinical distinctions between these three different results which may follow the entrance of bacteria into a wound are, however, more apparent than real, and the term septicæmia must be regarded as relative only; for it is highly probable that in sapræmia some bacteria do become carried off from the local lesion into the blood stream. In any given case it is often impossible, on clinical grounds, in the early stages to decide with certainty which variety of septic disease is present, and even later the line of demarcation may be very fine—indeed, the likelihood of other forms of septic mischief arising from the same cause must be constantly borne in mind.

Treatment

1. **General.**—The assistance of experienced nurses is one of the first essentials in the successful treatment of all cases of severe infection; in few conditions does so much depend upon the nurse in charge, not only for the immediate well-being of the patient, but also in the early recognition of some of the many complications which may arise. A second essential is an abundance of fresh air; the room, therefore, should be large, and the bed arranged as near the open window as is consistent with the avoidance of draught, or, whenever possible, should be pushed on to a balcony, the patient being protected by screens from draught; here, except, perhaps, in the coldest weather, the whole time may be spent, the patient being moved in only for washing, etc. For heavy patients an air- or water-bed is desirable. Septicæmic patients generally require propping up in bed, and the clothes should be light and warm. Bedsores form with great rapidity in this condition, and in order to avoid them the back and bony prominences and also the hair must receive most careful attention. The condition of the mouth also requires great care; if very foul, hydrogen peroxide is an excellent cleanser, while Listerine may be employed as a routine. A daily action of the bowels must be ensured, and the amount of urine passed in the twenty-four hours should be recorded.

(a) *Diet.*—The patient must be encouraged to take as much food as possible. When severely ill, milk, diluted, forms the chief article of the dietary, and an adult should take at least three pints in the twenty-four hours. The milk may be given plain, partly as milk jelly, junket, Benger's, or flavoured with coffee or tea. Barley water may be used as a diluent; soda-water is best avoided on account of its tendency to cause flatulence. In addition to the milk, three or more eggs should be taken—either beaten up in milk, or as boiled or baked custard, or as egg flip. Raw meat-juice, beef-tea, Brand's essence or Bovril, with a liberal addition of salt, should be given daily in small quantity. It should be remembered that a high temperature alone is no contra-indication to a liberal diet, and if the patient will take them, fish and chicken may be allowed throughout with a small quantity of alcohol, either as brandy (3 oz.) or stout or port wine. Feeds should be given every three hours, but the patient should on no account be wakened for a feed at night—though, if very ill, he will not sleep for longer than three hours at a time—and the amount lost may be easily made up later.

(b) *Drugs.*—Few drugs are required in the routine treatment, for the needs of no two cases are alike. Half an ounce of Ol. Ricini should be given as soon as possible. and in order to counteract the tendency of the stools to become offensive, an intestinal antiseptic, such as Izal oil (2 min.) or naphthalene tetrachloride (5 gr.) in capsules may be given twice a day. A mixture containing Tr. Digitalis (5 min.) should be given three times daily as soon as the diagnosis of septicæmia is made.

Several drugs have been employed in the hope of increasing the resisting powers of the body, unfortunately with little effect. Among such are collargol, nuclein, formalin and iodine, which have been injected intravenously.

2. **Local.**—The indication is to clean up as thoroughly as possible the local site of invasion, removing all foreign material in which the causal organisms flourish and abound, but in so doing to avoid as far as possible injury to the surrounding tissues. Efficient drainage must be secured, and the infected area should be freely irrigated with a mild antiseptic solution at a temperature of 100° F. For offensive wounds peroxide of hydrogen (5 vols.), potassium permanganate (1 in 1000), or tincture of iodine (1 oz. to 1 pint) are useful. For irrigation of cavities, such as the uterus, certain pro-

prietary products allied to carbolic acid—Lysol, Lysoform or Izal (1 in 200) may be employed. Douching of cavities may be followed speedily by a rise of temperature with or without a definite rigor; hæmorrhage, when it occurs, is usually slight. Normal saline solution is especially useful in dealing with large wound surfaces, and the tissues may be further cleansed by loosely packing with gauze soaked in 4 per cent. saline. The douche or irrigation should be frequently repeated; in the case of a superficial surface a bath may be employed for an hour or so at a time, fomentations being applied in the interval, but care must be taken lest the part become sodden through too-prolonged immersion. In bad cases the wound may be dressed with gauze soaked in normal horse serum or the appropriate anti-serum; this is of especial value when the infecting agent is one of the pyogenic cocci, or when the wound is slow to heal and granulations are late in appearing.

In cases of pure *sapræmia* this local treatment is usually followed by rapid improvement in the symptoms, but in *septicæmia* may lead to little or no amelioration of the patient's condition. The condition of the original wound in cases of septicæmia varies greatly. In some instances it may have healed completely, or show no marked local changes; but more frequently it is suppurating with raised inflamed margins, or there may be great swelling, much pain and marked lymphangitis. If small it should be excised; when situated on an extremity amputation may be necessary in order to save life. In not a few cases, chiefly those of streptococcal origin, the site of invasion may be obscure, the infecting organism gaining entrance through the middle ear, cranial air sinuses, mouth, biliary passages, intestinal tract or genito-urinary organs.

In *pyæmia*, if the infected area can be reached, the thrombosed veins should be excised and ligatured to prevent further embolism. Staphylococcal cases are not infrequently secondary to osteomyelitis and run a very rapid course; free incision must be made at once, and if widespread disease of medulla and periosteum is found, amputation performed without delay; when a doubtful area of inflammation is incised any exuding fluid should be taken, without exception, for bacteriological examination. If incision alone is performed in these cases of osteomyelitis, a positive blood-culture after the operation is a sure sign that amputation is imperative.

In the course of a pyæmia a sharp look-out must always be kept for the development of secondary abscesses, which begin to appear commonly between the fifth and tenth day. They are specially prone to occur in the lungs, spleen, kidneys, eye, joints, brain and areas subjected to pressure. In streptococcal cases the large joints are not infrequently involved; if treated by free and early evacuation of the pus little permanent damage may result. Occasionally such arthritis may subside without suppuration. Pathological dislocation is prevented by the application of splints, and later, massage. In staphylococcal infection the pleura, pericardium, kidneys and heart muscle are often affected. In the so-called chronic pyæmia multiple abscesses are met with, chiefly in the joints and cellular tissues. In all cases, except in moribund patients, the abscess should be opened as soon as detected; but in the lung the infarcted area is occasionally coughed up. Even after the fever has terminated and all local signs have disappeared, unless the patient puts on flesh and steadily gains strength, the greatest care must be exercised lest any surgical condition be overlooked. Especially when the patient has been treated with a vaccine, an abscess may form without any pain or tenderness, but will rapidly heal when the pus is evacuated.

One of the most rapid and satisfactory means at our disposal of assisting the body to be rid of the *toxæmia* is the subcutaneous or intravenous injection of freshly prepared sterile normal saline solution. It has the additional advantage of improving cardiac action and relieving thirst. One or more pints may be injected subcutaneously into the tissues of the flank or chest; more rapid absorption is obtained by introducing the fluid, as Woodman advises, through a Southey's canula inserted with the trocar vertically through the anterior axillary fold, the point of the canula coming to lie beneath the skin in the axilla. By this means two pints of fluid may be delivered in twenty minutes, leaving practically no swelling and causing very little pain when once the canula is inserted. A pint or thirty ounces may be injected into the median basilic vein in the cubital fossa; for this purpose a syringe with a three-way stopcock is the best to employ, as it does away with the necessity of cutting down to expose the vein, the needle being inserted just as in doing a blood-culture. The injection may be repeated daily so long as is necessary.

3. **Of Certain Special Symptoms.**—*Fever* of itself is not a serious sign, and an attempt to control it is only to be made when it makes the patient restless, or when it reaches a height above 104° F., which experience has shown may be associated with damage to the nervous system. The methods of control which are applicable are—

(*a*) Cradling, or ice cradling.

(*b*) Sponging with hot, tepid or cold water. The former is the more valuable, as it promotes surface evaporation.

(*c*) Wet packs—to be reserved for hyperpyrexia.

(*d*) Drugs. Fever is as a rule very little influenced by drugs, of which the most serviceable are quinine and cryogenin. The latter may be given in doses of 5 gr., three hourly, for three doses. In a *rigor* half an ounce of brandy in hot water is given as soon as the shivering begins, followed by hot coffee or milk. A hot blanket and well-protected hot-water bottles should be placed next to the patient, with extra blankets on the top. During the rigor the pulse may become imperceptible, but unless it remains impalpable at the wrist for more than three quarters of an hour, there is, as a rule, no cause for alarm. Should it remain absent for more than this time, a hypodermic injection of adrenalin (5 min. of 1 in 1000 solution), or pituitary extract ($\frac{1}{4}$ gr. = 1 ampoule, B. W. & Co.), or Liq. Strychninæ (5 min.) is required. In the rare event of these measures failing to restore the pulse, intravenous infusion of a pint of normal saline at a temperature of 100° F. will be necessary.

Sleeplessness is a serious symptom, and no effort must be spared in order to ensure plenty of sleep. Septicæmic patients are invariably "nervous" and apprehensive, and restlessness is often very marked. If not dependent on pain or any other obvious cause, alteration of the position of the patient in bed may be sufficient. Hot sponging is often efficacious, but has the great disadvantage of causing considerable inconvenience to the patient, and cannot be repeated. Hot milk or cocoa, an alkaline draught, hot whisky or brandy should be tried before resorting to drugs. Bromide and chloral hydrate, 10 gr. of each, may be given, repeated in an hour if necessary; sulphonal, heroin and nepenthe may be tried. Paraldehyde, given with gin or parmesan cheese is the safest of all soporifics in this condition. If sleeplessness is consequent on cough, 10–15 gr. of Dover's powder is often efficient. For pain in a wound, when aspirin and local applications of heat fail, a hypodermic injection of morphia with atropin will be necessary, but morphia should be withheld as long as possible, and if albuminuria be present, opium and its derivatives must be given with great caution.

Anæmia.—In septicæmia a steady fall in the number of the red cells is a very grave sign, and is met with especially when the infecting organism is streptococcus pyogenes. For its prevention a preparation of iron may be given by the mouth; but when hæmolysis is established it is preferable, in the majority of cases, to give a solution containing a grain of arsenite of iron hypodermically once or twice a day, with hæmoglobin (5 gr. t.d.s.) and extra-raw meat-juice by the mouth.

Distension.—The rectal tube may be employed for half an hour or so, four hourly. If this fails an enema of turpentine, or of asafœtida, or a mixture of both, should be tried. In addition to either measure, a hypodermic injection of physostigmine sulphate, or salicylate ($\frac{1}{100}$ gr.) may be given, and repeated four hourly for four doses.

Vomiting may be an early sign of peritonitis. If this cause can be excluded, give castor oil to begin with, followed by Sod. Bicarb., 1 dr., in $\frac{1}{2}$ pint of hot water. The quantity of milk must be diminished, and further diluted with lime water, barley water or coffee. Koumiss No. 1 may be substituted for the milk. Meat extracts are often retained when other foods are returned. If these measures fail, a mustard poultice or leaf applied to the epigastrium, or Tr. Iodi, 1 min. in $\frac{1}{2}$ oz. of water, may be tried every hour, for twelve doses, if required. In persistent vomiting it is necessary to stop all nourishment by the mouth and give a solution of glucose (1 oz. to 1 pint) either subcutaneously or by the rectum. When the vomiting ceases, a mixture containing hydrocyanic acid and bismuth salicylate may be helpful.

Diarrhœa may be of toxic origin, or due to some dietary indiscretion. The former is of serious import; Ol. Ricini, $\frac{1}{2}$ oz., Tr. Opii, 5 min., with brandy, 2 dr., should be given at once. The Izal oil may be increased to 4 min. four hourly. The diet must be diluted, and cold milky articles, sour milk, lime water or black coffee given. Raw arrowroot made to a paste with water and brandy, 2 dr. is often very efficacious. If the symptom persists, a starch and opium enema or rectal lavage with boracic lotion may be tried.

Cough.—The patient should be turned every two hours, to prevent pulmonary œdema. Hot milk or lemon drinks, liquorice lozenges or a heroin linctus will often afford relief. A well-made linseed poultice is the best application for pain in the chest, and is greatly to be preferred to leeches in these septic conditions.

Cardiac Failure.—It is on this that the fatal event in a septicæmia often depends. At the earliest sign of dilatation of the heart the quantity of brandy given in the twenty-four hours is to be increased to 4 oz., $\frac{1}{2}$ oz. being given three hourly, or, if the patient prefers it, an equal volume of champagne. When other circumstances allow it, the foot of the bed should be raised. Caffein sometimes works well, but is apt to cause insomnia. In "acute" failure, Curschman's solution (camphor 2, ether 1, olive oil, 7) 10–15 min. hypodermically, can be kept on for a long time at four-hourly intervals. Pituitary extract, $\frac{1}{4}$ gr. (1 ampoule, B. W. & Co.), is more lasting in its effect than Adrenalin, 5 min. (1 in 1000). The heart's action is often greatly improved by the administration of saline, or

better still of Ringer's solution (Soloid Saline Co. No. 2, B. W. & Co.) either subcutaneously or intravenously (*v. s.*).

Thrombosis of veins in the extremities, not infective in origin, occasionally occurs. The affected limb should be immobolised on a pillow between sandbags, the bed-clothes being raised over a cradle. The pain may be relieved by hot fomentations, or by painting with a mixture of equal parts of camphor, menthol and chloral. After six weeks, gentle massage with passive movements may be started.

Suppression of Urine and Renal Infarction.—The application of hot cloths and fomentations to the loins may serve to re-establish the urinary flow. If this fails, dry cupping and saline infusion may be tried. Caffein and theocin sodium acetate are not desirable on account of the extra strain they throw on the kidney. In renal infarction, urotropine, 10 gr., in water, 5 oz., may be given with citrates three times a day.

Specific Treatment

A valuable addition to the above methods of treatment lies in the employment of the appropriate vaccine or anti-serum, or both. A *vaccine* is a suspension of dead bacteria in normal saline solution. An *autogenous vaccine* is one prepared from the micro-organism isolated from the infected individual himself. A *stock vaccine* is one prepared from an organism isolated from a similar case of infection. A *sensitised vaccine* is a suspension in saline of a micro-organism which has been in contact with its specific anti-serum—a combination is thereby formed between the bacterium and its antibody, with the result that after its administration the "negative phase" is largely eliminated, so that larger doses may be employed, leading to an increased development of immunity. Such sensitised vaccine may be prepared from the organism isolated from the patient, *i. e.* autogenous, or "stock."

An *anti-serum* is one obtained from an animal, usually a horse, highly immunised against a particular organism, or group of organisms or toxin, by repeated injection therewith.

Before specific treatment—that is, treatment by vaccine or antisera—is carried out, exact diagnosis from a bacteriological point of view is essential. The methods of identifying a bacterial infection are—

1. *Direct*—that is, the isolation of the causal organism, or—

2. *Indirect*—that is, the identification of a specific antibody.

The former is by far the more valuable and can always be employed in cases of *septicæmia* and *pyæmia.* Films and cultures are made from the original wound or focus, where possible, especially from beneath a scab. In taking cultures from the uterus, or other cavity, the greatest care must be exercised lest material other than that from the infected site is obtained. For this purpose, the employment of some simple apparatus, such as Western's modification of Döderlein's speculum is helpful. This consists of a tube, capped at one end with thin rubber, sliding within another tube; the whole being sterilised before use. The outer tube is passed through the cervix, the inner being then inserted, while the platinum wire is finally passed through the rubber into the uterine cavity, all danger of contamination being thereby avoided.

The film preparation must on no account be omitted, for from its examination is determined the nature, varieties and relative abundance of the organism or organisms present, and the method to be adopted in the making of cultures.

Occasionally the wound at which the micro-organism has gained entrance has healed before the onset of septicæmic symptoms; in such cases it should be opened with strict aseptic precautions, and any fluid found—whether serous or purulent—taken for cultivation. In the event of failure at the initial site of infection, or where that is contaminated by the presence of a large variety of bacteria, the lymph glands draining the area, if enlarged and readily accessible, should be punctured with a needle attached to a hypodermic syringe and any juice obtained cultivated.

In *pyæmia*, the causal microbe may usually be isolated without difficulty from a secondary focus of suppuration, where previous efforts have proved unsuccessful. If these means fail, a blood-culture must be undertaken—and it is only in this way that the existence of a septicæmia, and its nature if present, can with certainty be established.

In those cases in which the site of invasion is not at once apparent, any such condition as suppuration in the middle ear or cranial air sinuses, cholecystitis, appendicitis or pyelitis must be carefully excluded as a possible source of infection.

Vaccine Treatment.—With regard to the dosage and frequency of administration of a vaccine in cases of septicæmia and pyæmia, a careful consideration of the general clinical condition of the patient must be the chief guide. In general, the more acute the case and the more widespread the infection, the smaller should be the dose employed. The doses given here are those which have been used in the treatment of average adult cases, the vaccine being given hypodermically in all instances. Serum and vaccine are often given coincidently with marked benefit.

If an ordinary vaccine is employed in *strepto-*

coccal septicæmia, the initial dose should not exceed 25 million, which if all goes well, may be repeated in four days; subsequently the dose is increased. At St. Bartholomew's Hospital considerable success has attended the use of *sensitised vaccine* in the treatment of streptococcal septicæmia. Its introduction is, however, too recent for any definite expression of opinion to be made as to its value. To an adult, three doses of 100, 250 and 1000 million are given subcutaneously on successive days as soon as the diagnosis is made. The toxicity of the organism being so largely neutralised in the process of sensitisation, this relatively large dose gives rise to very slight reaction.

Staphylococci are sensitised with difficulty; the initial dose of an unsensitised vaccine may be 50 million, repeated four days later and subsequently increased.

Though septicæmia is commonly due to infection by either a streptococcus or staphylococcus pyogenes, other micro-organisms are occasionally responsible for the condition. Such, for example, are the gonococcus, colon bacillus and influenza bacillus. In the treatment of these generalised infections by vaccine, the initial dose should not exceed 5 million; an injection may be given on three successive days of 5, 10 and 25 million. The gonococcus and colon bacillus can be "sensitised," but so far no serum is available for sensitising the influenza bacillus.

The general condition of the patient may show marked improvement under the influence of vaccine, without there being any coincident fall in the temperature.

Serum Treatment is of especial use in combating infections due to the pyogenic cocci. The serum may be administered by a variety of routes. The healing of unhealthy callous wounds is often expedited by dressing them with gauze soaked in normal horse or specific antiserum, and after any surgical measure, such as clearing out the uterus, anti-streptococcus serum may be applied to the raw area. The *intravenous* administration of serum should be reserved for those cases in which the full effect of the dose is immediately required; anti-streptococcus pyogenes — not polyvalent — serum, given by this route early in a case of streptococcus septicæmia is not infrequently followed by very great improvement in the symptoms, but later in the course of the disease the effect is less marked. Intravenous injection of serum is not uncommonly followed within half an hour by a rigor, and in such conditions as puerperal septicæmia, when there is already a septic thrombosis of veins, the inoculation may prove the starting-point of a series of perhaps daily rigors, where such have been absent before. Twenty-five or fifty c.c. are given in a pint of normal saline solution—freshly distilled water is essential in the preparation of the latter. If the *subcutaneous* route is chosen, 25 c.c. may be injected daily with strict aseptic precautions. The possibility of anaphylactic shock arising should always be borne in mind, especially when the dose is given intravenously to a patient who has been treated with serum before. In cases of *puerperal infection* the routine treatment at St. Bartholomew's is as follows: If the temperature rises and the uterus is at all bulky, before the lochia become offensive an anæsthetic is given and the uterus explored. Films are made from the uterine contents and immediately examined; cultures on blood-agar are taken at the same time. If a streptococcus is found in the film, a blood-culture is made, and 25 c.c. anti-streptococcus pyogenes serum in a pint of normal saline is given intravenously, followed by two subcutaneous injections of 25 c.c. at intervals of twelve hours. Should the temperature remain above normal after clearing out the uterus, a three-day course of stock sensitised streptococcus pyogenes vaccine is given as well. The cultures, if positive, are always kept, though an autogenous sensitised vaccine is but rarely employed.

If sensitised vaccine is available it is well to give it straight away; but if the patient is suffering from profound toxic effects, the indication is rather for serum, but in such instances it is advisable to give sensitised vaccine as well, for the effect of the serum is short-lived. If, however, there is no marked toxæmia sensitised vaccine alone has often proved sufficient.

When sensitised vaccine is not available, good effects have been known to follow the administration of vaccine and serum together—10 million killed cocci and 25 c.c. antiserum being injected subcutaneously. A. E. G.

RHEUMATIC FEVER

As rheumatic fever is now regarded as the result of infection by a specific organism, the treatment which is common to the acute specific fevers should be carried out, save that isolation is not required. During the whole of the febrile stage, and for some time afterwards, the patient should be kept in bed, in a large and well-ventilated room with a steady temperature of from 60° to 62° F. The body and bed-clothes should be sufficiently thick to prevent any chilling of the body, and preferably the patient will lie in a flannel sleeping-suit and between blankets. As sweating is often a marked feature, and is to be encouraged, the skin should be sponged with hot water at least twice a day, and the water may be rendered alkaline by the addition of carbonate of soda.

The body flannels must be changed as often as they become damp from the perspiration, so as to avoid the risk of a surface chill.

The toilet of the throat and mouth must be attended to by the free use of some mild antiseptic lotion containing boracic acid, or listerine, or Condy's fluid. In those cases in which the gums or the tonsils are in an unhealthy condition, local disinfection by means of carbolic acid, or Izal, or boroglyceride must be carried out during the illness. Owing to the arthritic pain usually present the question of complete rest in bed is easily settled in the case of adults, but in the case of children pain in the limbs may be trifling. It is none the less essential in all cases to maintain complete rest in the recumbent position through the whole of the pyrexial stage.

As thirst is usually present, water should be given freely. It is one of the best means of encouraging elimination of the poison. Potash water, thin barley water, lemonade or imperial drink flavoured with lemon or barley sugar are all admissible, and may be used according to the patient's preference.

During the pyrexial stage the diet should be fluid and light and given at regular intervals, say, every two or three hours. There should be no attempt to feed up the patient. Milk and water, Benger's food and milk, chicken-tea, and strained vegetable soups give a sufficient variety. Beef-tea, meat essences and meat jellies are better avoided. A cup of weak tea is probably harmless and is found to be very refreshing by most patients. Alcohol is better avoided save in the case of patients who are debilitated from other causes.

The **medicinal treatment** of rheumatic fever is of great importance because we have in salicylate of soda a drug which has a much more specific action than is attainable in the case of most fevers. Formerly the alkaline treatment prevailed and large doses of the salts of sodium and potassium were given, but it was difficult to determine any precise benefit from their use. The definite action of salicylate of soda in lowering the temperature, relieving the pain, and reducing the effusion into the joints is undoubted. This is a matter of everyday experience, but yet the specific action of the salicylate is denied by some. It is no mere antipyretic action, because not only is the fever permanently reduced in the majority of cases, but the arthritic pain and effusion are also removed. So reliable is the action of the salicylate that if I do not obtain this definite improvement within two or three days I begin to doubt the correctness of my diagnosis, and suspect the existence of pyæmia, or septicæmia, or acute rheumatoid arthritis. Again, it is sometimes stated that although certain symptoms of rheumatic fever are relieved by salicylates, carditis is neither prevented nor cured by their means. As a matter of clinical experience it will be found that carditis does not usually develop in a patient treated early with full doses of salicylate of soda. The very marked tendency in rheumatic infection to inflammation of the heart is well known, and the serious effects of this complication are an everyday experience in practice, but such effects are not common in those cases which have been treated early and thoroughly and sufficiently long in the acute stage of rheumatism with salicylate of soda.

Always keeping in view the liability to rheumatic carditis we shall probably find that our two best preventive measures are complete rest and salicylate of soda. The cure of rheumatic carditis by salicylates is another question. While an active pericarditis will often subside as the direct result of salicylate treatment we cannot observe the same result in a damaged valve or myocardium. But these damaged tissues will certainly be placed in a much better position for recovery by supplying them with blood freed from rheumatic toxins and organisms, and this is best produced by means of salicylates. While we do not expect such a marked effect in active valvulitis or myocarditis as in some other rheumatic lesions, we must not be deterred from persisting with the salicylate treatment in such cases. The old view that salicylates did harm in the case of active carditis has now been dropped as no evidence was forthcoming of any such result. It has probably occurred to others, as to myself, to find an active recurrence of rheumatic symptoms in a patient who had been relieved of all symptoms by means of salicylate of soda and who was still taking the drug. I do not know the explanation of this, but I have seen a similar occurrence in cases of syphilis, where marked benefit was being obtained by means of mercury and yet fresh lesions occurred during the treatment. Such occurrences are too exceptional to shake our belief in the efficiency of well-tried drugs like mercury and salicylate of soda.

The administration of salicylate of soda should be begun as early as possible in the attack. For an adult from 90 to 120 gr. in the course of twenty-four hours, and for a child of ten from 40 to 60 gr. will be sufficient in the majority of cases. The medicine should be administered every four hours in doses of 15 to 20 gr., and within forty-eight hours the temperature will probably have reached normal. When this stage has been reached the dose may be reduced to two-thirds, and in a few days to one-half of the original amount. The exact dose required must be determined accord-

ing to the conditions present in the patient. In a severe attack in a healthy subject it may be advisable to push the drug at an early stage, giving 20 gr. every two hours until some effect has been produced on the fever and pain. It is not advisable to discontinue the drug on the cessation of fever and other active symptoms. One aims at eliminating the poison as completely as possible from the system, and for this purpose the salicylate should be continued to the amount of a drachm daily for some weeks. It is a good rule to keep on with the drug as long as the patient is in bed, but I believe it is also beneficial to intermit the use of the salicylate for a few days at a time during this period. Custom has lately favoured the addition of an alkali, such as bicarbonate of soda, to the salicylate in doses equal to or double the amount of the latter drug. It has been advised with a view to prevent the symptoms of acidosis or acid intoxication which sometimes followed the administration of salicylates. As marked acidity of the urine is also characteristic of rheumatic fever the free use of alkalies is probably beneficial. I do not think that enormous doses of bicarbonate of soda are required, but that from one to two drachms in the day, in combination with the salicylate of soda, will be found to be beneficial in the acute stage and smaller doses in the convalescent stage. Enough has probably been given when a slight alkalinity of the urine is maintained. As rheumatic fever is sometimes characterised by relapses, recourse should be had at once to full doses of salicylate of soda and an alkali on a recurrence of fever or joint pains.

As a rule salicylate of soda is well tolerated, but some patients suffer early from nausea, vomiting and depression. When the disturbance appears to be gastro-intestinal in origin, an attempt may be made to remedy this by giving the dose more frequently and in smaller amounts at a time, 5 to 10 gr. every two hours, well diluted with water. In some cases it may be found that the drug is impure and has caused the gastric disturbance. The natural salt is preferred by some to the synthetic preparation, and while it may suit better those patients with gastric intolerance, for general purposes the synthetic preparation has been found quite efficient. Intolerance of the salicylate may be manifested early by headache and buzzing in the ears. This is undoubtedly an idiosyncrasy in certain people, more especially those of the neurotic temperament. In such cases salicin in 15 gr. doses or acetyl-salicylic acid in 10 gr. doses may be tried. As regards the general use of acetyl-salicylic acid in the routine treatment of rheumatic fever I cannot find that it has any advantage over salicylate of soda. Its chief characteristic, the relief of pain, may be taken advantage of in specially painful forms of the disease by giving it occasionally in place of the dose of salicylate of soda. There are certain drawbacks to the use of acetyl-salicylic acid. It is very insoluble in water and it is broken up in the presence of an alkali. Under the name of aspirin it is largely used as a domestic remedy for headache and pains of all kinds, and the physician may suffer in the estimation of the patient if he employs such a common remedy.

A valuable paper on the subject of the action of salicylic acid and organically allied bodies in rheumatic fever by Prof. Ralph Stockman has appeared recently (*Brit. Med. Journal*, 1913, I. 597), and the following observations are taken from this reliable source. *Benzoic acid* or *sodium benzoate* given in 15 to 20 gr. doses hourly or two hourly is effective, and its action is similar to that of salicylate of soda, but very much weaker. *Salicylic acid* in 15 or 20 gr. doses every four hours may be regarded as equally efficacious with salicylate of soda, but the latter has the advantages of being more soluble and less irritating to the stomach. *Saligenin* is chemically the alcohol of which salicylic acid is the corresponding acid. He treated four cases with it in doses of 10 gr. every two hours, and found its action to be rapid and satisfactory. A good deal of perspiration followed its use and two of the cases suffered from deafness. *Salicin* is the glucoside of saligenin and yields only 43 per cent. of its weight of salicylic acid, so that the necessary dose is twice as large as that of salicylate of soda. Given in 20 gr. doses hourly or 30 gr. every two or three hours, its action in rheumatic fever is highly satisfactory. On the other hand, Dr. Stockman found that a number of drugs when given in medicinal doses were quite ineffective in rheumatic fever. Amongst these may be mentioned *phenol*, *salol*, *quinine salicylate*, *glycosal* and *cinnamic acid*. The reason of the uselessness of these drugs he traces to the absence or small amount of salicylic acid which they contain or which they develop in the body.

Within recent years it has been asserted that salicylate of soda is not usually given in sufficiently large doses to obtain the greatest benefit. The amount recommended has been from 200 to 400 gr. daily, and even larger amounts have been employed. The dangers in connection with excessive doses of salicylate of soda are admitted by all who have used them. In many cases the patient is seized with sickness and vomiting and so escapes the risk of poisoning. In other cases the drug is excreted so rapidly by the kidneys that no harm follows,

but if the kidneys are functionally impaired the risk is a real one. If the drug is retained in the system, the tendency to acid intoxication is always present, especially in the young, and a fatal issue will so definitely follow the continued use of the drug that elaborate precautions have to be taken to avoid this. It is recommended that from 400 to 800 gr. of an alkali (bicarbonate of soda) should be given daily to counteract the tendency to acid poisoning, and that the salicylate should not be given when the bowels are constipated or the kidneys are not acting freely. In a hospital, with resident physicians and nurses watching the patient day and night, such precautions may be carried out, but in private practice one does not want to run unnecessary risks, and the use of salicylate of soda in moderate doses calls for no such watching of the patient, and no such antidotes along with the drug.

Local Treatment.—As a rule the acute symptoms yield so readily to complete rest and salicylate treatment that local measures are now much less called for than formerly. When the joints are much inflamed and swollen and the fibrous aponeuroses generally are involved the sensitiveness of the patient may be so extreme that even the pressure of the bedclothes or a movement of the bed causes great suffering. It is advisable in such cases to have a long cage over the patient, protecting the trunk and limbs from any pressure. The swollen joints should be swathed in a thick roll of cotton-wool. If any one joint is specially painful, hot fomentations, sprinkled with laudanum or tincture of belladonna, may be applied at intervals. Blisters about the joint and local applications of salicylic compounds have been employed formerly, but are of little value as compared with the internal administration of salicylate of soda.

Serum Treatment.—Various efforts have been made to provide an efficient serum in this disease, but so far without much success. A serum has been prepared by Menzer, and he claims to have obtained better results from it than from any other form of treatment. So far his results have not been confirmed by others. Vaccine treatment has not led to any definite results, and this may be due primarily to the fact that the specific organism of rheumatic fever has not been discovered. While the *micrococcus rheumaticus* of Poynton and Paine may be the cause of the disease, it would appear to be an elusive type of organism which does not lend itself readily to the production of an effective therapeutic vaccine.

Complications.—In treating a case of rheumatic fever the physician always bears in mind the possibility of complications, and by far the most common and most important of these is inflammation of the heart. The carditis of rheumatism is, as a rule, an infection of the heart generally, but symptomatically the brunt of the infection may appear to fall on the pericardium, or the endocardium, or the myocardium. Whichever part may seem to be involved, and however slightly, it is a good rule to regard the case as one of cardiac infection, and therefore requiring more prolonged treatment than one in which the heart has escaped. The latency of cardiac disease must also be kept in mind, so that attention must be directed to the heart all through the convalescent stage, and even when the patient has been out of bed, in order to see how it responds to increased effort. More especially in the case of children are these precautions necessary, for it is in early life that the tendency to rheumatic heart disease is greatest. In the absence of well-marked evidences of cardiac involvement suspicion should always be aroused by a persistently rapid pulse, by cardiac dilatation, or by a faint mitral murmur.

If the heart is found to be involved the treatment must be carried out on general lines, for we have no means at present of directly treating acute carditis. The same measures are to be adopted whether the lesion is apparently endocardial or myocardial or pericardial. The great measure we have to fall back on is rest, perfect rest of mind and body, so that the circulation may go on in a steady uninterrupted manner, and the natural disappearance of the inflammation may take place under the most favourable conditions. The duration of the rest after an attack of rheumatic fever is to be regulated by the progress of the cardiac lesion. We naturally desire as regards the heart a *restitutio ad integrum*, and this will be manifested by a regular pulse of normal rate, an absence of dilatation, and the disappearance of endo- or peri-cardial murmurs. The time necessary may have to be counted by months rather than by weeks, and the process may be extremely tedious to the patient, but the important thing to realise is that at no time will the opportunity ever recur of treating the acute carditis and its effects successfully. We may not be able to secure complete healing, but we shall at least secure a minimum of permanent damage. Other measures tending to eliminate the poison should be persevered with, such as those acting on the skin, the bowels, and the kidneys. I do not know of any medicine which will affect the carditis. Digitalis is certainly useless in cases of recent inflammation of the heart and is probably harmful. Iodide of potash, and grey powder, in small doses, are still believed in as useful eliminants, and I

think may at times be useful. The pain of pericarditis may produce so much unrest in the patient that it must be relieved. For this purpose hot fomentations or leeches to the præcordium may prove helpful, but the free use of morphia is probably the most effective treatment.

A somewhat rare complication of rheumatic fever is hyperpyrexia, which is always serious, probably more from the intense toxæmia of which it is a sign than from the degree of fever. If the temperature rises above 106° F. an effort should be made to lower it by means of hot packs or packing ice round the patient. The general condition of the patient must be kept in mind and active measures directed to the hyperpyrexia should not entail great disturbance and exhaustion of the invalid. The administration of hot drinks and hot brandy and water are also useful, while antipyretic drugs probably do more harm than good.

The *convalescent stage* calls for some consideration. A liberal diet is to be allowed of nutritious and digestible foods. A fresh attack will often be induced by over-feeding, so that special attention should be paid to the condition of the digestive organs. If they are sound a mixed dietary of beef, mutton, fowl, fish, green vegetables, puddings and eggs may be allowed. Constipation must be avoided by the use of cascara or senna pods. A condition of anæmia usually follows an attack of rheumatic fever, whether cardiac disease has been present or not. It is not advisable to try to relieve this by large doses of iron, which will probably only have the effect of inducing a recurrence of indigestion and rheumatic pains. The anæmia will usually yield to the influence of diet, of green vegetables more especially, and of fresh air and sunlight.

A first attack of rheumatism, treated under favourable conditions, will usually be recovered from. In the case of adults there may be no further trouble, but in the case of children there is always a risk of recurrence, either in the form of a fresh attack of rheumatic fever, or in the more insidious form of rheumatic manifestations, such as tonsillitis, "growing pains," erythema, subcutaneous nodules, chorea, pericarditis or pleurisy. Any one of these forms may not be recognised as rheumatic and may escape treatment, with the result that fresh and progressive inflammation of the heart takes place. It is, therefore, a good plan after an attack of rheumatic fever in a young subject to continue the regular use of salicylate of soda for one or two years. The patient may be ordered to take at the beginning of each month 20–40 gr. of salicylate of soda daily for a week. By this means future trouble of a serious nature may often be avoided. G. A. S.

ANTHRAX, RABIES AND GLANDERS

Anthrax

The anthrax bacillus is not responsible at the present time for a large variety of lesions in this country, and these are limited almost entirely to the districts where trades in imported hides are carried on. By far the commonest lesion is the malignant pustule, or as it is more correctly termed, cutaneous anthrax. Other lesions are found in the lungs and intestine, but pulmonary and intestinal anthrax are very rare, and, as a rule, are not discovered until a post-mortem examination is made. If such are to be treated, an early recognition of the condition can only be made by a careful bacteriological investigation of the respective excreta in all cases of acute pulmonary and intestinal affections occurring in districts where there is a possibility of infection. In cutaneous anthrax the lesion is, as a rule, characteristic, but in all cases the diagnosis requires confirmation by the bacteriologist. In the treatment of cutaneous anthrax there are three methods suggested as being efficacious; the older methods of incision and simple cauterisation having been almost abandoned.

The methods are—

1. Expectant treatment.
2. Excision of the lesion.
3. Serum-therapy.

The two latter may be used in combination. Many observers hold that the expectant method alone is justifiable, and that a cure will result in the majority of cases. The statistics of all cases treated in this country contra-indicate the adoption of this plan.

In examining the records of all cases that have been dealt with in this country since 1905 it will be seen that excision of the lesion is the method of treatment which most often averts a fatal issue. In carrying out excision, it is essential that the whole of the lesion, together with a good surrounding margin, should be extirpated, and the resulting wound allowed to granulate up, with or without the application of nitric or pure carbolic acids or other caustics.

At the same time this method of treatment is not always the most convenient, for it so happens that the commonest site on the skin for the appearance of the lesion is on the face just below the margin of the orbit, a situation where it is not always possible efficiently to carry out complete excision.

Moreover, it is apt to produce so severe a scar that such conditions as ectropion are liable to follow the healing of the wound, and to produce marked disfigurement. The period of convalescence demanded by such a method of

healing has, moreover, to be considered, since it is among the working-classes that infection takes place.

Serum-therapy has to a large extent replaced the above methods. The type of serum used is that introduced by Sclavo, which was first brought into this country by Legge. The method consists in the injection of large doses into the subcutaneous tissues, the smallest initial dose being no less than 40 c.c. If the first dose does not bring about the desired result, injections of 20 c.c. may have to be repeated daily.

The immediate effects of the treatment are variable, both on the general condition of the patient and on the local lesion. Sometimes there is no obvious change, at others the temperature rises within the next twenty-four hours to 103–105°, and occasionally a rigor follows. Headache, malaise and nausea are common sequels.

The lesion may remain as before, or there may be a considerable increase in the area of inflammation around the local focus. Both of these effects, however, clear up with forty-eight hours, ofttimes sooner, and the patient speedily becomes convalescent. Anthrax bacilli almost always disappear from the lesion within eighteen to forty-eight hours. Statistics show that if the condition is diagnosed early this treatment is as efficacious as excision; and it has the advantage that there is usually very little scarring and no large granulating surface from which secondary septic infections may result.

Again the period of isolation is considerably diminished, as the patient may return to his work within a few days, instead of weeks, since he is no longer infectious.

A combination of the use of serum therapy with excision is advisable in the more severe lesions. Serum therapy is the only possible method of treatment for the pulmonary and intestinal types of the disease when diagnosed.

No harm has so far been observed in the use of the serum, and it has even been given intravenously together with normal saline solution without harmful effect. As to prophylaxis, all bedding, bed-clothes, towels, etc., should be burned, since the disease is spread by the spores of the bacillus. All feeding utensils and the like should be specially sterilised by prolonged heat at high temperatures; touching of the lesions with the fingers should never be allowed.

Rabies

Hydrophobia is a disease which has become almost extinct in this country. Isolated cases, however, are met with from time to time.

Its treatment comprises prophylaxis and active treatment. The former method consists in immediate attention to a bite produced by a suspected animal. The wound, if possible, should be excised completely, and combined with the application of the thermo-cautery, pure carbolic acid, nitric acid or silver nitrate.

As a rule there is no advantage in doing this if the lesion has been present for some time, as the toxin spreads up the nerve sheaths to the central nervous system. During the incubation period, which varies from five days to six months, the average period being about forty days, some method of immunisation should be adopted.

The Pasteur method of immunisation is the favourite one. This consists in the introduction of a vaccine in daily doses subcutaneously. The vaccine is prepared from the dried spinal cords of rabbits which have been infected with the virus, starting with attenuated virus obtained by drying for a period of fourteen days; and each successive dose being obtained from cords dried a shorter period is of increased potency. The highest strength is, as a rule, prepared from a cord dried for three days. The process of inoculation lasts for fourteen days. An intensive method is also used in which the process is carried out in eight days, a toxin of greater potency being employed for the first dose.

By the use of this method the death-rate has been reduced from 10 to 1 per cent. For success it must be adopted at the earliest possible stage.

Serum therapy has also been advocated by Tizzoni, and it is alleged that cures take place even after the symptoms of the disease have appeared. This serum is prepared by immunising sheep with the attenuated virus. The virus is attenuated by the Italian method of treating the infected rabbits' cords with gastric juice. The dosage of the serum is 10, 5, 5 c.c., given on three successive days.

More recently Marie has succeeded in producing a sensitised vaccine, *i. e.* the emulsion of the infected rabbit's cord is mixed with antirabic serum, the latter being removed by washing with normal saline solution after they have been in contact for twenty-four hours. It has the advantage of producing immunity more rapidly than the method used by Pasteur.

Glanders

The infections due to the Bacillus Mallei are fortunately rarely seen among human beings. Stablemen and persons dealing with infected horses or other animals, and pathological investigators are most liable. The result is almost invariably fatal in acute cases, but in the more chronic forms a certain number recover. The treatment consists in the giving of stimulants liberally, and the use of certain drugs such as iodine, arsenic or creosote.

In the pulmonary and intestinal types little can be done locally. An attempt should be made to disinfect the initial site of infection. When this occurs in the nasal mucosa, washes should be frequently given with the application of caustics to any ulcers that may manifest themselves.

If the focus is in the skin, abscesses should be opened, nodes or ulcers excised, disinfectants such as the mercury salts or zinc chloride applied, or the actual cautery used. No anti-serum has yet been prepared, but vaccine therapy has been adopted, though with little success.

Great care should be taken in isolating an infected patient, as dissemination from one individual to another readily occurs. The same care should be adopted in identifying and killing the infecting animal, and the stables should be submitted to a very thorough process of disinfection. W. G. B.

TETANUS

1. **Prophylactic Treatment.**—In the great majority of cases, tetanus is caused by an earth-infected wound, and burns appear to be particularly liable to give rise to it, at any rate in America. Great care should be taken, therefore, to cleanse thoroughly any such wound. Unfortunately this is not a certain protection. In several cases in a series recently studied by the writer, tetanus supervened in spite of careful cleansing and the use of antiseptics. It is probably wise to employ Lister's "strong lotion" (carbolic acid 1 in 20 + solution of $HgCl_2$ 1 in 500), for dirty wounds. Even this will not kill tetanus spores in a short time, but if the other germs are killed tetanus bacilli do not usually produce any symptoms.

It has been advised to inject a prophylactic dose of antitetanic serum whenever one has to deal with an earth-infected wound. This advice appears to be sound, for in animals protection can usually be obtained in this way. The results of giving the serum *before* symptoms appear are far better than when the patient is already in convulsions. Nevertheless, there are about twenty cases on record in which tetanus has supervened in spite of the prophylactic injection. The writer has seen one case in which the serum itself produced symptoms exactly like tetanus within twenty-four hours, but the patient recovered. Apparently most of the individuals who developed the disease notwithstanding a precautionary dose of serum have recovered (six out of eight recorded).

It must never be forgotten that the bacilli may be introduced during surgical operations by infected instruments or catgut. The only safety lies in boiling for more than fifteen minutes; nothing less than this can be relied upon to kill tetanus spores. Iodine catgut is safe. The theory has recently been advanced that post-operative tetanus is due to an infection from the alimentary canal.

A remarkable means by which the disease may be lighted up into activity is by the intramuscular injection of quinine. It has long been known that tetanus may follow this treatment, and the sterility of the needle was suspected, but it is now shown that lurking bacilli, unable to produce symptoms because unaccompanied by cocci, may have virulence conferred upon them after the quinine injection. This has been verified in animals. Quinine ought, therefore, only to be given by the mouth except in cases of urgency.

When the symptoms of tetanus have already manifested themselves, the prognosis depends more upon the nature of the infection than upon the mode of treatment adopted. In acute cases the mortality is about 83 per cent., in milder or chronic cases about 43·6 per cent. (Jacobson). Of thirty-one cases at the Bristol Royal Infirmary nine recovered, but in three or four of these there was no wound discovered. The more difficult it is to find a cause, the better the outlook. In our cases, the leg and foot wounds gave a better prognosis than those of the arm, and all the head cases died; tetanus toxin travels by the nerves, so that the longer the nervous route the better the prognosis. The incubation period gives some clue to the result; of patients whose symptoms arose in ten days or less, only one out of twelve recovered, but of eleven cases with a longer incubation period four got well. It has been known from the time of Hippocrates that if a patient survives the fifth day of symptoms he has at least an even chance of recovery, and our figures bore this out. In appraising the value of the treatment adopted in reported cures of tetanus, the incubation period is very important; when it is long the patient would probably have recovered anyhow.

2. **Treatment of Declared Tetanus.**—Three cardinal principles have to be observed, to remove the focus whence the toxin is absorbed, to combat the infection of the nerve cells, and to relieve the symptoms.

(a) *Removal of the Affected Area.*—If there is an obvious wound, which will probably be quietly suppurating, it should be cut out *en masse* under an anæsthetic, or burnt out thoroughly with the cautery, without loss of time. It is no use trifling with antiseptics, which will not kill the spores unless used as caustics.

(b) *Antagonising the Infection of Nerve Cells.*—The majority of surgeons have come to the conclusion that antitetanic serum given by the

ordinary means and in the ordinary doses has been tried and found wanting. Even in experimental animals it meets with little success after symptoms have developed. Although antitoxin is able to neutralise tetanus toxin, it has but little if any power to disrupt the union between the toxin and the protoplasm of nerve cells.

Nevertheless, it is customary to inject 20 to 30 c.c. daily into the subcutaneous tissues of the abdomen, in the hope that further infection may be averted. The injection is made with an antitoxin syringe which has been boiled, the skin being prepared by painting with tincture of iodine or other suitable method. The puncture is sealed with collodion. Septic complications are very uncommon, but it is well to cover with an aseptic dressing for a day or two.

Attempts have been made to obtain better results by greatly increasing the dose of the serum. In a small series of twenty American cases treated with injections of 500 c.c., it is claimed that as many as 75 per cent. of the patients have been saved, but they appear to have had a mild type of the disease. Still, large doses are worth a trial, and the writer has seen one quite severe case saved by this treatment combined with the injection of magnesium sulphate. The large doses are quite harmless.

Another device which has been recommended is to give the antitoxin into the brain, or vertebral canal. In the former method of treatment, a trephine hole is made over the frontal lobe and the needle plunged into the cerebral substance. This procedure has been followed by abscess of the brain, and is not likely to come into favour. It is claimed by some American writers, notably by Rogers, that better results are obtained by injecting the serum through a lumbar puncture into the spinal theca amongst the nerves of the cauda equina. Seven cases are quoted, of whom four recovered, in which Rogers gave 10 to 20 c.c. subcutaneously, with the same dose intravenously, 5 to 20 minims into the great nerve trunks, and 10 to 20 c.c. into the cauda equina, deliberately aiming at penetrating the nerves. One would wish to be very sure that the antitoxic serum was aseptic before running this risk, or the patient's slender chance of recovery might be further jeopardised by meningitis.

Baccelli's Phenol Injections.—If statistics could be relied upon, infinitely the best results have been obtained by this method. In Italy it appears to be the routine treatment. Baccelli reports ninety-four "severe" cases, of whom only two died, and another series of thirty-eight "very severe" cases, of which sixteen died. But these figures are collected from published cases, which is misleading, as it is only the successes that are likely to get into print. The method has been tried two or three times at the Bristol Royal Infirmary without success, but it is simple and harmless, and might well be used as a routine. It appears to have saved some quite severe cases.

Hypodermic injections of a 3 per cent. solution are given every two or three hours. The initial doses contain about 3 gr. of phenol, and it is aimed to get in as much as 30–45 gr. in twenty-four hours. Carboluria will probably occur, but may be neglected.

The theory is, of course, that the bacilli are killed by the carbolic acid, but this is open to doubt, and the sedative action probably helps.

The Russian Method.—Krokiewicz, acting on the principle that tetanus toxin has an affinity for nervous matter, seeks to divert part of its activity by giving injections into the subcutaneous tissues of sheep's brain. This is made up into an emulsion with normal saline, 10 gr. being given in 30 c.c. of saline (150 gr. in 1 oz.) every other day. Of sixteen cases, eight being described as severe, thirteen are reported to have recovered.

(c) *Symptomatic Treatment. Intraspinal Injection of Magnesium Sulphate.*—Meltzer observed that in experimental animals magnesium salts would inhibit spasms of spinal origin, and for this reason he introduced the method into therapeutics. It is usual to give 3 c.c. of a 25 per cent. boiled solution of magnesium sulphate by injection into the vertebral canal in the lower lumbar region. Probably smaller doses would serve the purpose. The injection is repeated every day. There is often produced a very high tension of cerebro-spinal fluid in consequence of the osmotic pressure of the salt, and in that case it is probably wise to let some drain away at the second and third puncture. The patient's head must be kept raised.

We have no large or reliable body of statistics to guide us in appraising this method, and at the best it is only symptomatic, but the personal impressions of a number of British and American surgeons are rather favourable. The writer believes that he has seen it do good. Phillips records four recoveries in his seven cases, and collects from the literature twenty-eight cases, of which sixteen recovered. The method is not altogether free from risk; one fatal case is recorded and in another artificial respiration was necessary; bronchorrhœa may follow.

Sedatives.—All the sedative drugs have been tried in the treatment of tetanus, and they probably allay the pain even if they do not control the spasms. In the Franco-German War the German surgeons considered that curare gave the best results, but it is seldom used now. Morphine relieves the pain, but does not

check the spasms, and usually fails to induce sleep. Chloral and bromides probably give better results. When swallowing is difficult, they should be given in full doses per rectum. Inhalation of chloroform may be desirable when the convulsive attacks are long and severe; it will control them for the time being, but should not be kept up for longer than half an hour once or twice a day.

The **general management** of a case of tetanus calls for a few remarks. The patient should be isolated in a quiet darkened room with as little coming and going as possible. The bowels, which are often very confined, may be kept open once in two or three days with drop doses of croton oil, but calomel, 5 gr. at a time, should be tried first. If swallowing becomes difficult, fluids may be given with a feeding-cup, or if necessary a rubber tube may be passed down the throat through a gap in the teeth. If passing it causes spasms it may be left *in situ*.

Some Italian authors believe that hot bathing is a valuable means of allaying the spasms.

3. **General Summary.**—In the writer's opinion the measures to be taken are as follows—

A prophylactic dose of antitoxin (20 to 30 c.c.) should be given when there is an earth-infected wound, at any rate in countries where tetanus is common. Thorough cleansing with "strong lotion" should be used at once.

In mild cases of tetanus, with an incubation period of a fortnight or more or with no obvious wound, in which the spasms are infrequent and not severe, give sedatives, and 30 c.c. of antitoxin subcutaneously, repeated if the spasms recur. Isolate the patient. Even if it is probable that recovery will take place it is wise to give antitetanic serum in all but the mildest cases showing only trismus but no wound and no spasms, because sometimes symptoms which begin mildly pass into fatal manifestations of the disease later on. The wound, if any, should be excised or thoroughly cleaned up with strong antiseptics.

In severe cases, the patient ought to be isolated, the wound excised, and sedatives administered. If an antitoxic serum of guaranteed sterility can be obtained, inject 10 c.c. into the spinal theca by lumbar puncture, or 20 c.c. intravenously by means of a needle and funnel into the median basilic or other prominent vein. Sterilise the skin with tincture of iodine or spirit and biniodide, and make the vein prominent by tying a bandage round above it. Take care to inject no air bubbles, and remove the bandage when the needle is safely inside the vein. The serum may be diluted with 50 c.c. of warm saline. Unfortunately one cannot safely inject large doses of the albumins of blood of another species.

Further, the patient should be given 300 to 500 c.c. of antitoxin subcutaneously, in two or three places, by means of needles and a funnel.

If there are severe spasms, Meltzer's magnesium sulphate ought to be given by lumbar puncture.

In the absence of antitetanic serum, in cases where it cannot be afforded, or when it has been given as above described on the first day, and there is no marked improvement, Baccelli's carbolic acid injections ought to be given a trial, because although the statistical evidence is so compiled as to be unduly favourable, the method has undoubtedly cured some quite severe cases after antitoxin had failed to effect any improvement.

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A. R. S.

GONOCOCCAL INFECTIONS

Abortive Treatment.—The abortive treatment should only be attempted if the patient comes for advice within four days after contracting the disease, and provided the subjective symptoms are slight only. The treatment should consist in washing out the anterior part of the urethra twice a day with about a pint of a 5 per cent. solution of protargol, or a 25 per cent. solution of argyrol, or a 1 per cent. solution of hegonon. The treatment should not be continued for more than three days, and if it has been successful no gonococci should be present on the fourth day.

Unfortunately patients seldom come for advice soon enough, but if a case can be obtained before the discharge is copious or the patient has a burning pain on passing water the abortive treatment will almost invariably prove successful. Putting the patient to bed during the course will materially assist the treatment.

Practical Differences between Anterior and Posterior Urethritis

The great difference between acute anterior and posterior urethritis rests in the fact that, owing to the collection of pus in the prostatic portion of the urethra and its passage along the path of least resistance, which is over the neck of the bladder into the bladder itself, so much irritation is set up, that in acute posterior urethritis the patient is always requiring to pass water, and has to get up three or four times or more in the night to do so.

If the two-glass test is used, owing to the pus mixing with the urine in the bladder both portions will be thick. If the pus collects in the urethra only, then the urine passed in the first glass will be thick, while that passed in the second glass will be clear.

If both portions are thick and the patient does not have to get up in the night to micturate, the thickness is either due to phosphates or urates: the former will disappear on adding acetic acid and the latter on heating.

The two-glass test is not of much use in chronic cases, because in whichever part of the urethra the lesion is situated the threads brushed away therefrom will only appear in the first glass. If threads are seen in the second glass, they usually come from the prostate.

Speaking generally, long threads are urethral, short threads and dots are prostatic. A urethroscopic examination will show in which part of the urethra there is inflammation.

Treatment of Acute Urethritis

1. **Hygienic.**—First of all rest, both to the part—by wearing a suspensory bandage—and to the person. Bed is seldom necessary, but active exercise must be forbidden. Alcohol should be strictly avoided, and hot foods and condiments—mustard, pepper, sauces, etc.—should not be taken. Excessive smoking has not infrequently aggravated the disease.

2. **Symptomatic.**—Pain on passing water can generally be diminished by diluting the urine by drinking more milk and water, or barley water and alkaline mineral waters, Evian water in particular. Decreasing the acidity of the urine by drinking lime water often affords relief. For the acute pain caused by spasm of the compressor urethræ muscle, nothing is better than a warm hip bath or a hot opiate fomentation, which at the same time relieves the retention, if present. If there is hæmaturia the patient should remain in bed until hæmorrhage has stopped, and cold evaporating lotions should be applied to the penis, and sodium salicylate given internally.

3. **Local.**—Two courses are open: giving by the mouth such drugs as are excreted through the urethra and direct application of drugs to the urethra itself. The drugs usually given internally are resins and balsams like cubebs, copaiba, sandal-wood oil, etc., the last being the best; but all are of very little value and less useful than the well-known mistura alba, which keeps the bowels well open—a most important point in the treatment of gonorrhœa. In acute posterior urethritis nothing is better than sodium salicylate.

A mixture which finds favour with some is the following—

℞ Copaibæ ♏ xv
Pulv. Cubebæ gr. xxx
Pot. Iod. (in increasing doses) beginning gr. x
Sp. Ætheris Nitrosi ♏ xv
Mucilag. Acaciæ ʒ i
Infus. Taraxaci vel. Buchu ad ℥i.

When this mixture is given, twice daily injections of a 1 in 10–20 solution of perhydrol (Merck) should be ordered. The theory is that the H_2O_2 liberates the iodine from the potassium iodide, and allows the free iodine to exert its destructive action upon the gonococci.

The local application of the proprietary preparation known as "Iodex" is now under trial, and would appear to give favourable results. For direct application to the urethra, potassium permanganate 1 in 4000 or until the solution is the colour of red blotting paper is the best drug. If a silver salt is desired, preference should be given to a 0·1–0·3 per cent. solution of hegonon. It should always be remembered that every salt of silver should be freshly prepared, and that whatever drug is employed more harm can be done by using too strong than too weak a solution.

No injections should be given until the pain on micturition as well as all redness and œdema of the penis have disappeared. They should then be employed twice daily until every trace of the discharge has ceased, and for at least ten days after. In quite a large number of cases this will result in cure. The old fear of driving the disease back by using injections is not supported by practical experience. In anterior urethritis the solution injected goes only as far back as the triangular ligament and returns through the meatus.

Acute Posterior Urethritis.—In order to wash out the whole of the urethra and bladder, which is necessary in acute posterior urethritis, either the column of fluid to be injected must be raised higher, or the return opening in the glass tube must be stopped up. It is far better to wash out the urethra and bladder with a cannula just inserted into the meatal orifice, than by passing an instrument directly into the bladder, because it is so easy to injure an inflamed mucous membrane, and through the abrasion so caused, the gonococci may reach the systemic circulation.

Chronic Urethritis.—The anterior part of the urethra is rarely affected alone; when such is the case, twice daily injections of a 0·1–0·3 per cent. solution of albargin will speedily effect a cure; if it does not, then the presence of a para-urethral canal must be considered. These canals may or may not communicate with the urethra internally, but they usually open externally in the region of the corona glandis

or in the glans penis just external to the meatal orifice. They may be unilateral or bilateral, and are usually about 3 cm. or more in length. They can only be closed by electrolysis, which is accomplished by inserting a fine platinum needle attached to the negative pole, and passing a current through it of 1–2 ma., for one to two minutes.

Another cause of chronic or recurring anterior urethritis is inflammation of the bulbo-urethral glands. The secretion should be expressed by massage and then an injection of a 0·5 per cent. solution of silver nitrate given per urethram. A chronic or recurring urethritis is most commonly posterior and dependent upon either inflammation of the prostate or the seminal vesicles. Massage per rectum of these structures, continued with instillations per urethram by means of an Ultzmann's syringe of 1 or 2 c.c. of a 0·5 per cent. of silver nitrate, or 5 per cent. solution of copper sulphate will sometimes result in a cure. It must be remembered that the mere presence of threads in the urine does not always signify an active or even latent gonococcal infection, because many patients who have had frequent attacks or who have been treated with too strong solutions may have threads in the urine for the remainder of their days. A cure cannot be ascertained by searching for gonococci, since in many cases a chronic urethritis may be kept up by the diphtheroids, staphylococci and streptococci, which have long since exterminated the gonococci. These secondarily infected cases are usually made worse by the injection of fluids which have a specific anti-gonococcal action, and only clear up when the silver salts are supplanted by very weak solutions of biniodide or perchloride of mercury. The best method of diagnosing a chronic gonococcal urethritis is to give a large dose of a potent gonococcal vaccine, and if there are gonococci latent, the injection will quickly stir them up, with the result that within forty-eight hours the patient will either have had an increase in the urethral secretion on rising or even a profuse discharge. The further administration of vaccines may cure such a case, especially if the prostate or the seminal vesicles are affected. Many a case of urethritis is kept up by a stricture, and no treatment short of gradual dilatation or urethrotomy will effect a cure.

Gonococcal abscesses along the penis should be treated as long as possible with cold evaporating lotions and rest; the knife should only be used when they actually point, and then only the smallest incision should be made just sufficient to let out the pus. A urinary fistula may result, but it will almost invariably close of its own accord in time, and operative interference is seldom called for.

Many a case of acute prostatis will resolve by merely putting the patient to bed and inserting a psychophore per rectum, through which runs a stream of cold water. A prostatic abscess frequently bursts into the urethra and brings about a spontaneous cure; if it points into the rectum, only a tiny incision should be made to evacuate the pus. Resolution is rapid and a fistula is extremely rare.

Gonococcal Cystitis so rarely occurs, and when it does the infection becomes so quickly superseded by the bacillus coli that the treatment does not differ from that which is described elsewhere.

Epididymitis, on the other hand, is an extremely common complication, and, as when bilateral it is a frequent cause of sterility, may call for special and energetic treatment. Some few cases will resolve under rest in bed and local applications of Lotio Plumbi or Ichthyol, with sodium salicylate internally, but if a case is seen early it is better to employ either of the following two methods of treatment—preferably the former.

1. Take the scrotum into one hand, make the skin tense over the epididymis and plunge a scalpel into its substance, in its long axis, in two or three places; the pain is momentary, but the relief which so quickly sets in is enormous. Then treat in the usual way with lotions, etc.

2. Inject into the epididymis 1–2 c.c. of electrargol. The epididymis reaches its normal size in one to three days, and only occasionally is a second injection necessary.

Paraphimosis occurs mechanically and is not due to the patient having drawn back his foreskin and being afterwards unable to draw it forwards again. Attempts at reposition frequently fail, then the treatment is either to divide the constricting band or better to remove the incarcerated portion of skin and stitch the edges together. If necrosis has already occurred the less done the better; the parts should be kept clean with antiseptic lotions and powders should be freely used to keep the necrosed area as dry as possible, leaving the rest to nature.

Systemic Complications.—The commonest are iritis and arthritis, and it is in such conditions that vaccines are most useful, but local treatment should never be omitted, and special attention should be paid to the genital tract. In the case of iritis, atropine should be used, in the case of arthritis, sodium salicylate with potassium iodide should be given internally, and a 10 to 40 per cent. guaiacol ointment should be applied externally. Atophan is sometimes very useful and can be prescribed as follows—

℞ Atophan
Sod. Bicarb. āā gr. vii
M. f. pulv. in cachet.

One cachet to be taken before every meal.

The addition of guaiacol carbonate may be helpful.

Venereal Warts, gonorrhœal warts or condylomata acuminata, are hypertrophic masses of epithelium produced by inflammation in the corium. The inflammation is not caused by the gonococcus, but by the bacterial flora which collects and flourishes in the corona glandis. Keeping the area perfectly dry with powders will often result in their spontaneous disappearance; this is the best treatment when there are many. If there are only a few, it is best to scrape them away with a Volkmann's spoon and to paint the base with silver nitrate stick, which both sterilises the surface and stops the bleeding.

Gonorrhœal Ophthalmia.—(1.) *Infantile.*—Prophylaxis is the chief point, and that can only be effected by keeping the mother's genitals as clean as possible, and by bathing the baby's eyes immediately after birth with a 2 per cent. solution of silver nitrate, or a 10 per cent. solution of argyrol. It is well to wash out the silver solution by some normal saline.

(2). *Adult.*—The affected eye must be protected at once with a Buller's shield, which is an ordinary watch glass retained in position by a piece of adhesive plaster. The eye should be frequently washed with a solution of a silver salt, atropine drops must be used to prevent adhesion of the iris, and leeches applied to the temple to reduce inflammation.

Vaccines.—A vaccine to be potent must be prepared, without the employment of heat, from a fresh culture, or the first sub-culture which has not been allowed to grow for more than forty-eight hours. The vaccine should be fresh, as it begins to deteriorate after the tenth day, even when kept in the dark at 0° C. No evidence is forthcoming that an autogenous vaccine is to be preferred to a heterogeneous. There are three different methods of employing vaccines: (1) Ordinary vaccine given subcutaneously or intramuscularly; (2) autolysed vaccine given intravenously; (3) sensitised vaccine given subcutaneously or intramuscularly. Of these three the last is the best, because, provided the immune serum used for sensitisation contains anti-endotoxine, no negative phase follows its employment and the patient does not suffer from toxic symptoms (for full details see *Journ. Path. and Bact.*, 1913, Vol. XVII. 559).

Ordinary Vaccine.—The initial dose should not exceed 5 million, and the second dose of the same size should not be given for ten days or more; and each subsequent injection of very gradually increasing doses should not be given more than every seven or ten days.

Intravenous Autolysed Vaccine.—The therapeutic effect is better than that obtained by the preceding method, but as many injections are required, toxic symptoms may often occur. The initial dose should be 1 to 3 million given in 5 oz. of saline; the succeeding doses should gradually be increased up to 15 million, and not given oftener than once a week.

Sensitised Vaccines.—Injections should be given on three successive days in doses of 20, 50 and 100 million. If the patient has no reaction, doses of 200, 500 and 1000 million may be prescribed on the fourth, fifth and sixth days. Should a reaction appear after any one of these, fourteen to twenty-one days should elapse before a further series are given.

The sensitised vaccines are most useful in acute cases treated early, and speedily effect a cure. Chronic cases may often be improved enormously by vaccines, but after they are stopped the disease remains latent for a time, only to break out again; therefore a cure should not be guaranteed.

In cases of arthritis where there is much fluid in the joint, tapping is often necessary, after which a Martin's bandage should be applied to prevent refilling. Injecting the fluid drawn off subcutaneously has often been advised, but it seldom does much good. (For further details see article on *Chronic Diseases of Joints.*)

Autogenous vaccines made from the organisms which have been grown from the expressed secretion from the prostate, which contain staphylococci, streptococci and diphtheroids, may occasionally be beneficial when the gonococcal vaccines have failed.

Vaccines in Women and Children.—Although vaccines will frequently banish the symptoms of a cervicitis and endometritis they will not cure the case, unless local treatment is also prescribed. The pains which salpingitis produces will likewise disappear under vaccine treatment, but the majority of cases recur in time. Gonococcal joint affections, which are commoner in women than is suspected, yield very well to vaccines.

Women always seem to be more affected by vaccines than men, and owing to the marked reaction which may occur in them after gonococcal vaccines, namely, increase of pains, menorrhagia and metorrhagia, it is advisable to use sensitised vaccines.

Children.—Joint affections respond admirably to vaccines, but the vulvovaginitis which is always the first symptom, and by far the most troublesome, is in the majority of cases quite uninfluenced. Vaccines should therefore only be tried in obstinate cases as an adjunct to systematic local treatment.

J. E. R. McD.

CHOLERA

The essential principles in the treatment of Asiatic Cholera are: (1) to replace as soon as

possible the fluid and salts lost from the blood through the copious evacuations, so as fully to restore the circulation and the renal functions, thus producing an excretion of the toxins already absorbed; (2) to destroy the poisons formed in the bowel, thus cutting short the disease.

Estimations should be made of the specific gravity of the blood and of blood pressure to reveal the amount of fluid lost from the system and the degree of collapse. The former can most conveniently be found by means of series of small bottles of glycerine and water from 1,042, 1,044, etc., up to 1,070, which can be made up with the help of an accurate hydrometer. The bottle in which a small drop of the finger blood just floats for a second or two has the specific gravity of the blood, or if it sinks in 1,064, but rises in 1,066, then the intermediate figure is the correct one. The rectal as well as the surface temperature should also be taken on admission.

Methods of Replacing the Lost Fluid.—In the first place water and barley water should be given freely by the mouth in small quantities at a time, vomiting not being a contra-indication, as some toxins are thus removed. Half a pint of normal saline (90 gr. of sodium chloride in a pint) should be given by the bowel every two hours, and in mild cases this may suffice to prevent collapse and save the necessity of more active measures. Saline has also been very largely given subcutaneously in cholera, but this is far inferior to the intravenous method, as it is painful and tedious to run sufficient quantities into the connective tissues. When used in the acute stage they should be hypertonic, as explained below. In an adult, up to three pints of sterile hypertonic saline can be rapidly given intraperitoneally by means of a special canula made for me by Down Bros., or by a small trocar and canula as successfully used by Bishop. This method is also inferior to the intravenous one, but as it is simpler and more rapid it may be valuable when the circumstances or the number of cases prohibit the use of intravenous injections. Lastly, we have the intravenous method by means of a canula tied into a vein at the elbow, or in small children over the internal malleolus. The vessel is fully exposed and incised transversely below, a forceps holding the anterior wall, so as to form a small flap, beneath which the canula is readily passed and tied into the vein, the distal portion of which has first been ligatured. The most convenient canula is a stop-cock one, with the end tapering slightly towards the point so as to enter a small vessel easily. In very young children a finer canula can be made by melting and drawing out the end of a small piece of glass tubing, while I have found that even puny infants can be transfused through the great saphenous vein at the ankle with the physiologist's fine glass canula for blood-pressure work. By using a glass bulb graduated in ounces the rate at which the fluid is entering the vein can be timed and regulated by means of the stop-cock.

When collapse is present in an adult three to four pints should be run in at the rate of a pint in five minutes, or four ounces per minute, to obtain a full pulse. When the specific gravity was originally 1,065 or over, an additional pint or two may be injected at the rate of one ounce per minute, if severe headache or oppression in the chest does not result, and if the patient is quiet and evidently relieved. In children of ten about one and a half pints may be given, less for younger subjects.

The Indications for an Intravenous Injection are: (1) If the pulse is very feeble at the wrist, the blood pressure below 80 mm., and the specific gravity over the normal figure of 1,056 to 1,058. (2) Whenever the specific gravity is raised to 1,063 or over (which means that at least three pints of fluid have been lost to the system), even if the blood pressure is over 80 mm., in order to anticipate and prevent the threatened collapse. (3) In the absence of the above guides severe cramps, restlessness, cold and blue extremities are in themselves safe indications for intravenous injections in cholera.

The *solution* should be hypertonic, containing 120 gr. of sodium chloride, 6 gr. of potassium chloride and 4 gr. of calcium chloride to a pint, soloids (B. W. & Co.) containing these proportions being on the market, four of which in a pint make the hypertonic solution and three an isotonic one. The *temperature* of the fluid, which must have been completely sterilised by boiling, should depend on the rectal temperature of the patient, and unless this is subnormal, as in a few very severe cases, it should not be above blood heat. If the rectal temperature is over 100° F. the saline should be injected at several degrees below blood heat, while if the rectal temperature is as high as 102°, I give the saline at the room temperature of the Calcutta hot and rainy seasons, namely from 80 to 85° F. I have in this way successfully transfused patients with a rectal temperature as high as 105 and 106°, who would certainly have died of hyperpyrexia without this precaution. If collapse again ensues, or the specific gravity of the blood rises to 1,063 or over, the hypertonic intravenous injection must be repeated, and in occasional cases even a third or fourth injection may be successful.

Destruction of Cholera Toxins in the Bowel by Permanganates.—I have shown by experiment that permanganates have the power of rapidly oxidising cholera toxins into harmless bodies,

while the small bowel is so empty in this disease that the drug can be given in sufficient quantities by the mouth in the form of keratin or salol coated pills to affect the course and mortality of the disease materially. In severe cases two pills, each containing 2 gr. of potassium permanganate, are given every quarter of an hour for two to four hours, and then every half hour until the stools become less copious and of a greenish or yellow colour. In milder cases and in children smaller quantities are given. In addition, a solution of calcium permanganate, of a strength of from 2–6 gr. to a pint is given to drink in large quantities. Commonly, in about six to eight hours the stools change colour, when the permanganates are omitted, but a further course of 16 gr. is given twenty-four hours after admission to guard against relapses, or whenever rice-water stools are again passed.

The Reaction or Febrile Stage of Cholera.—When the circulation of a cholera patient revives, either naturally or after an intravenous saline, the temperature rises usually to 102 or 104° F. This reaction must be carefully watched, and if the fever exceeds 104°, ice to the head, cold sponging and cold water enemata must be used immediately, for if the patient once becomes unconscious from hyperpyrexia I have never seen recovery take place, although a temperature of 106° is harmless if detected and reduced without delay. Restlessness and delirium after a transfusion are signs of dangerously high fever. Excessive reaction is most common in Europeans during very hot weather.

In the collapse stage of cholera no drugs except permanganates are of any use, as absorption is completely at a standstill. Opium in any form I have found to increase the mortality greatly, especially from uræmia, and I never allow it to be given in any patient whom I even suspect to be suffering from cholera. *Acids* were once largely used, but completely failed in the Hamburg outbreak, and I have also found them to increase the mortality. Intestinal disinfectants designed to kill the cholera organisms in the bowel have also signally failed. *Astringents* are not only useless but increase the danger of uræmia, and I never try to check the diarrhœa by their means, especially as I find that as soon as the renal secretion becomes free (say 2 pints in twenty-four hours), and the rectal salines can be safely omitted, the evacuations stop spontaneously. *Ammonia* in the form of sal volatile and ammonium carbonate is the best stimulant, being sometimes useful in the later stages, especially if there is any congestion of the lungs. *Alcohol* is injurious, increasing the vasomotor paralysis, and I never give it except to convalescents accustomed to its daily use, when champagne is the best form.

The Treatment of Deficient Renal Excretion.—By far the most difficult condition to deal with is the failure of the kidneys to resume their functions during the stage of reaction, as is common in patients in whom there has been persistent renal stasis during prolonged collapse before treatment began. In the first place the deficiency may be due to a continued high specific gravity of the blood, such as from 1,058 to 1,064, leaving too little fluid for the kidneys to act on. This is usually easily remedied by subcutaneous, or better slow intravenous, injections of 1 or 2 pints of normal saline (90 gr. of sodium chloride to a pint), which often suffices to increase the urinary excretion at once. Secondly, it may be due to continued low blood pressure, from vasomotor paralysis. This is a more serious condition, since in an adult male a pressure permanently much below 100 mm. nearly always results in fatal suppression of urine, especially after middle life. Salines may still be given cautiously if the specific gravity is not down to 1,050 or less, but vaso-constrictors and cardiac stimulants are of equal importance. Of the former adrenalin is sometimes useful at first, but pituitrin is more valuable on account of its prolonged steady action. In addition digitalis, or better strophanthin, which is said to dilate the renal vessels, and caffein-sodio-salicylate should be persisted with, while oxygen inhalations are worthy of trial. As the alkalinity of the blood is much reduced in the uræmic stage of cholera I have for some time given full doses of potassium citrate after the collapse stage is passed, with, I think, beneficial effect. Hot-air baths I have found to be too exhausting. All the above measures too often fail, and the greatest safeguard against the deadly uræmic complication is early and repeated intravenous salines to shorten the collapse stage with its dangerous renal stasis, which no doubt markedly damages the kidney epithelium. With previous organic disease of the kidney the chances of recovery are greatly reduced.

Diet.—The most essential point in diet is to avoid giving any form of animal albumen, from which toxins can be readily elaborated by the comma bacillus, during the first three days. Water and barley water only are allowed *ad libitum*. In favourable cases late on the third day a little arrowroot and whey may be cautiously tried, though relapses occasionally occur, which are usually recovered from on reverting to the former treatment. Next, citrated milk is allowed and the diet gradually increased. The patient must be kept recumbent, as late fatal syncope is not unknown.

The system of treatment which has been briefly outlined has reduced the death-rate from cholera in Calcutta and elsewhere to

considerably under one half of its former rate, and it is now rare to lose a previously healthy subject who comes under treatment during the first six hours of the attack. L. R.

TUBERCULOSIS

In following the progress of a parasitic disease, such as tuberculosis, we are watching a life-and-death struggle between two adversaries, the human body and the organism of the disease—here, the tubercle bacillus. When the physician is called upon to intervene, he is required to take no less a part than that of "second" or backer to one of the combatants—the human body—and to fill this important post with success it is necessary that he should know something of the adversaries and their mode of fighting. He must do more, as a rule, than merely stand by and see fair play—he cannot, indeed, like Mephistopheles, step in and give the fatal thrust, since he has not the needful weapon—we possess at present no chemical means of destroying the tubercle bacillus *in situ*. He can, however, back up, encourage, and to some extent train the human body to greater and better chosen exertions, and also, perhaps, supply it with weapons for the fight. To do this successfully he must first of all inform himself by what means and with what weapons victory over the tubercle bacillus can be obtained.

What do we know about the fight?

We know first of all that soon after the tubercle bacillus has got a foothold in the body, the body becomes "sensitive" to this organism, so that when fresh bacilli are introduced or tuberculin given, a "reaction"—the tuberculin reaction—tends to occur. This and the subsequent rebound is the body's response to further infection or spread of disease, and the means, in all probability, whereby natural cure takes place. Bacillary products passing out into the tissues cause a series of these slight reactions and thereby the defensive mechanism is aroused, protective substances are formed and, at the same time, a useful hyperæmia is set up in the foci of disease. Where, on the other hand, the dose is excessive, as in cases of acute or advanced tuberculosis (compare also the overdosage of the early tuberculin era) reactions run riot and the body is overcome—fever, wasting and general illness mark the effect of the tuberculous poison or nervous and other tissues and the end is at hand.

The position is strikingly similar to that which may occur in human combat. A blow with the fist, if moderate, elicits a smart return—a knock-out blow, on the other hand, or a series of quickly placed smaller ones, will lay out our man. How are we going to train him to oppose the tubercle bacillus?

Firstly, phthisis has small beginnings—we must discover our enemy at an early stage, an early diagnosis is of the first importance. At this stage the bacillus is a poor fighter, our man can oppose him with a little coaching, and if we keep him up to the mark, will gain a ready victory.

If the enemy has got stronger, the disease more advanced, our man must be put into training against a smaller adversary at first. This is where tuberculin comes in, the initial dose being minute and rising gradually as the body is trained to oppose it. If, finally, we are only called in when the adversary has gained the upper hand or at any rate a temporary victory, we must keep off the enemy as much as we can while our man gets his wind—auto-inoculation must be reduced to a minimum by "typhoid" rest in bed. We must then "pad" our man against the enemy's blows—must produce tolerance to tuberculin, the poison of the bacillus, by accustoming our patient to larger and larger doses. The body is thus hardened, as it were, to withstand the punishment it is bound to expect. If the disease is advanced this can be but a temporary triumph, but in earlier stages it may improve the health sufficiently to allow arrest or cure to come about.

We have now got an idea of the lines which rational treatment of tuberculosis must take. In the first place we have the general health of the body to raise and to maintain throughout the struggle at its highest level. In the second place we must train it in the special warfare needed to overcome the tubercle bacillus.

Our subject finds, then, a ready division into general and specific treatment.

General Treatment or Health Building

Tuberculosis is conveniently classified under the headings Local and Autotoxic—in the first division come cases where the disease is strictly localised and the general health unaffected; in the second, disease of wider spread or affecting vascular and mobile organs like the lung, so that some amount of general illness results. It is obvious that under either condition the general nutrition, and nervous energy, must be considered as of the first importance, but the remarks which follow will necessarily apply in the main to autotoxic disease, such as phthisis, where special measures have to be undertaken to raise and maintain the general health.

Hygienic-Dietetic Treatment.—This is the equivalent of sanatorium treatment, but may be taken to cover all other measures of a similar kind. It is, of course, the first and most vital step in the treatment of tuberculosis, and the form in which it is best administered in an individual case often taxes to the utmost the knowledge and ingenuity of the physician.

Sanatorium treatment expresses its highest development, for here, in addition to the most efficient arrangements for climate, air, sun, soil and suitable diet, we have the constant supervision of a doctor highly trained in this branch of work, and the opportunity of specific treatment being carried out in competent hands. The sanatorium is the best start-off for all who can afford it, as it gives opportunity for special investigation in cases which need it, is almost essential in febrile cases and is the best place in which to start a course of tuberculin treatment. Failing the sanatorium, or after return from one, home treatment in a well-arranged shelter, of which a large number of convenient patterns are now on the market,[1] or between well-ventilated rooms and garden, may form the nucleus of a successful cure. Dryness, sunshine, and protection from prevailing winds are the main points to consider in the selection of an outdoor site, since these are the factors which most of all favour continued and comfortable open-air existence.

The main factors of Hygienic-Dietetic treatment may be considered under the headings of the Open-Air Régime, Climate, Diet, Rest and Exercise.

Open-Air Régime.—The most valuable effect of open-air treatment is the influence it exerts on the spirits and appetite, digestion, and all the bodily processes. It increases tissue change and supplies nervous energy, and there is good reason to believe that this is mainly brought about by skin stimulation and heat demand. For this reason cold, dry air and hot sun by day, such as are found to perfection in certain mountain climates, are the best. Failing these, and where these are contra-indicated, the driest place available must be sought, the clothing must be porous and not too heavy, and skin stimulation from sun and air and cold bathing or sponging encouraged. The patient must not be allowed to live in a tropical morass under his clothes, which may well happen if the conditions required are not understood. Under a reasonable skin stimulation and the corresponding increase of nervous energy all the functions of the body are performed at a higher level, nutrition increases, and the body is better able to respond to the demand for the formation of antibodies against the tubercle bacillus. It is, perhaps, on this account that the open-air régime exerts such favourable effects on the symptoms, especially fever, associated with auto-toxic disease.

Open-air treatment should be carried out in the spirit, but not made a fetish. It must be remembered that stimulation is only of value as long as it leads to efficient response; prolonged chilling only exerts a depressing effect. The patient must be reasonably covered, should immediately change wet clothes, is best protected from fog and mist, and derives no benefit from draughts.

Avoidance of mixed infections is a further most important factor in the value of open-air treatment, and a very temporary relaxation of discipline may wholly neutralise this good effect. Thus a visit to friends in stuffy rooms, an evening entertainment, the introduction of a household catarrh, may render nugatory the effects of open-air isolation.

Climate.—Climatic influences are of value, but they must not be overrated. Recovery does not wait on locality, however suitable, but rather on the troublesome routine which a suitable climate can forward but never supplant. The fame of health resorts for phthisis has been earned by their physicians and the opportunities these have for supervising the lives of their patients rather than by climatic excellence. Open-air treatment may be carried out and carried out efficiently almost anywhere, but when a choice of locality exists it must be wisely exercised. A well-chosen climate should, in the first place, encourage the open-air régime; in the second place, it should supplement it where needful. This it will do mainly by its heat-abstracting powers, and these depend on temperature, humidity and wind conditions. In all cases the patient's power of response is the test of suitability, and to determine this it is necessary to inquire into his personal experience of climates and the effects of winter, summer, cold and heat upon him. The young and vigorous respond well to a large heat demand, and for them the high Alps are well suited; the elderly do not well meet the call for increased tissue change, and warmer and less vigorous climates are better. In all cases a dry air is most suitable, for with dryness are associated abundance of sunshine and cool or cold nights—the changes of temperature are large but well borne and less likely to chill the surface than are smaller changes in a moist atmosphere.

First on the list come the *mountain resorts*, where the cold rarefied air and powerful sun exert a maximal influence on nervous energy and respiratory exchange, and lead to increased assimilation and renewal of bodily vigour. The Swiss Alps are most convenient of access, and such places as Davos, Arosa and St. Moritz are well suited to vigorous patients, especially for the winter months, and are staffed by able physicians. Every case should be put in charge of one of these, and it must be remembered that not all cases can stand the Alpine climate; advanced disease, especially when accompanied by extensive laryngeal tuberculosis, much emphysema and kidney disease are distinct

[1] See *Brit. Journ. of Tuberculosis*, 1912, VI. 124–128; also advertisements in subsequent numbers.

contra-indications. After the mountain resorts come certain *low level climates*, suitable on account of dryness of air, abundance of sunshine and shelter from excessive wind. The Riviera represents the dry coast climate, but has certain disadvantages. Excessive wind and dust are serious drawbacks, but still more so the less complete medical control patients will submit to in this neighbourhood, and the social temptations to which they are exposed. Dry hot air is obtained in the *desert climates*, of which Egypt and the neighbourhood of Algiers supply the most notable examples. Those places are especially suitable for cases with bronchitis or bronchiectasis, emphysema or kidney disease, where the high and cold climates disagree; they are, unfortunately, only available during a short period of the year. Places with moist climates, such as Madeira, seldom suit phthisis patients; where, however, a very irritable laryngeal complication is present a moist and dustless climate may be given a trial. There is no greater danger to a phthisis patient than to develop a "wanderlust" in search of health; the belief that recovery lurks in some distant clime and cannot be found nearer home is a fatal error and must be opposed.

The *English climate*, though marred by excessive moisture and cloud, yet gives quite successful results in the open-air treatment of most cases of tuberculosis. Attention must be given, as we have said, to individual peculiarities and also to the nature of the disease. Hardy patients will do well on the east side during the summer months and even in the winter. The south is more sunny, but also of moister atmosphere, especially towards the west—Bournemouth, Ventnor and Torquay being the best known on this coast. Many cases do better at inland resorts than the sea. Fortunately, sanatoriums now exist in most parts of the country, and changes can be made for time of the year and other reasons. But it must be remembered that the medical officer is always a more important factor than the climate surrounding his station.

Diet.—Fortunately the days of forced feeding for phthisis are no longer with us. It is recognised at length that obesity is only of disadvantage by throwing more work on the lungs—moreover, the increased fat, water and flabby cells are not the best fitted to respond to stimulation by the production of antibodies against the tubercle bacillus. What we need is quality, not quantity; we must strive for the optimum of nutrition, not the maximum, which is something very different. This is not to say that a patient may not be brought above his original body weight with advantage, but only that his "condition" is at least of equal importance with his weight.

The diet in tuberculosis presents few particular points—it should be that best suited to achieve ample nutrition in the particular patient. Individual and national tastes must be studied, but the patient not allowed to become too faddy. A mixed diet with a good proportion of proteids and fats is the best. All forms of meat and fish may be given according to the patient's digestive powers, and eggs are a convenient stand-by when full quantities of other proteids cannot be taken. Milk may be given, when it agrees well, with breakfast and tea, and at bed-time, and perhaps in the middle of the morning. Preparations such as Malt Glidine or Plasmon may also be used as additions to meals where required. Fats are well taken where the climate is cold, but may need reduction in hot weather; they may be given as cream, butter, fat bacon, or beef or bacon dripping, and should be well broken up by being eaten with bread or similar vehicle.

Cod-liver oil is also readily digested by many patients and forms a convenient vehicle for creosote if desired. Alcohol should be considered purely as a stomachic, but where a glass of beer or light wine improves appetite and digestion it may be given with distinct advantage. Attention must be paid to efficient mastication and the teeth put in the best possible condition, not only with a view to this, but also to eliminate the dangers of mixed infection arising from this source. Pyorrhœa must be looked for and kept in control where present.

The patient should be weighed every week at the same hour and in the same clothes, and a record kept on the temperature chart. It must be seen that the patient is not unduly depressed when the weight refuses to rise, since this may react on the progress of a case otherwise favourable.

Rest and Exercise.—The rôle of rest and exercise in the treatment of tuberculosis is but too little appreciated. In an autotoxic disease such as phthisis their regulation is of vital importance, and in practice it constitutes one of the most difficult problems ever presented to the physician. The effect of exercise on the temperature, and to a less extent on the pulse, forms the basis of control, and the following indications must generally be followed—

Rest in bed is required as long as there is fever; in case the temperature is uncontrolled by ordinary rest, "typhoid" rest, in which movements are as completely restrained as in typhoid fever, must be given a trial.

Exercise must be begun on the level; at first, where there has been fever, for only five or ten minutes daily and increased very gradually each week till four to six hours a day are reached. Daily exercise must be decided

by the temperature chart—a rectal temperature of 98·8 or over on waking, or of 99·8 or over at 6 p.m. are indications for bed, and slighter rises will necessitate slighter restrictions, such as a shorter walk or rest in a chair. An occasional day in "bed" supplies a useful "rest" chart by which to control the effects of exercise, remembering always that no temperature should be taken within an hour of active exertion. All patients, in spite of their ability to take exercise, should have complete rest for half an hour before meals and for a short time after.

Lawrason-Brown suggests the following printed rules as an aid to the co-operation of the patient in the matter of exercise and rest.

Rules for Exercise.

(Exercise means walking. Special permission must be obtained before indulging in other forms of exercise.)

None for one week after beginning treatment, then ask about it.

None if feverish.
,, ,, blood in the sputum.
,, ,, loss of weight.
,, ,, the pulse is rapid.
Never get out of breath.
,, get tired.
,, run.
,, lift heavy weights.
No mountain climbing.
Go SLOW.
Exercise regularly and systematically whether rain or shine.
Walk up hill at start so as to come down hill on return.
Remember always that you will have to return.
Rest one half-hour before meals.

Accessory Treatment. General Tonic Treatment.—The hygienic-dietetic treatment may be forwarded in many cases by the exhibition of certain drugs. These act in the main as tonics, often through the digestive organs. A simple alkali and bitter before meals is helpful to the appetite and digestion, even apart from any dyspeptic complaint; if the appetite flags, a minute dose of zinc sulphate ($\frac{1}{6} - \frac{1}{4}$ gr.) in a couple of drachms of some bitter infusion is often invaluable. Creosote and its derivatives have been much favoured in phthisis and are useful in all forms of tuberculosis. In moderate doses given after meals they appear to stimulate digestive functions, but injudiciously pushed or given when stomach catarrh is present they may cause marked gastric irritation. Beechwood Creosote (1 min. increased up to 5 min.) may be given in cod-liver oil, and this makes an excellent mixture during the colder parts of the year. Otherwise it may be taken in sherry or put up in capsules. Guaiacol (1–5 min.) is its most useful derivative, and thiocol (5–10 or 15 gr.) dispensed in orange syrup diluted with water makes a useful preparation for children. Cinnamic acid, as the salt hetol, has been extensively tried in tuberculosis with the purpose of causing a leucocytosis, but no definite clinical success has followed its use. Recently, extensive claims have been made for a mixture called dioradin (radio-active menthol iodine) in the treatment of tuberculosis; it appears to have been useful in cases of surgical tuberculosis, but its value in phthisis still lacks proof. Pneumosan (amyl-thio-trimethylamine) has been given in phthisis and other forms of tuberculosis with apparent increase of nervous energy and therewith improvement in the general nutrition and pulmonary symptoms. It is interesting that trimethylamine is present in cod-liver oil, especially, it is said, in the cruder brown preparations. Such drugs as arsenic, best given, perhaps, as sodium cacodylate (1 gr.) by intramuscular injection so as not to disturb digestion, iron, and the hypophosphites, may all find a place as tonics in the general treatment of tuberculous patients.

Symptomatic Treatment. — Treatment must be directed, where possible, to any symptoms which are distinctly interfering with the progress of the case. Thus fever, apart from its significance, may upset digestion and appetite, cough may cause auto-inoculation and so fever, pain may hamper calm respiration and prevent sleep. In treating such symptoms great care must be taken that we do not check natural response but only control it; also that we do not exchange bad for worse, as, for example, by destroying appetite and digestion in the injudicious treatment of cough. In a short article like the present, only a few indications can be given under these headings.

Fever generally points to activity of disease. It is important to distinguish between fever and high temperature, which is only the sign manual of this. Treatment of fever is all important and means elimination of toxæmia. Treatment of high temperature is truly symptomatic, and should only be undertaken when as a symptom its prominence is interfering with progress. All measures to prevent auto-inoculation by "typhoid" rest and to diminish cough and unnecessary talking must be first employed. Some patients with fever, especially children, will take their meals well in spite of it. The food should be nourishing but lighter than for apyretic patients, and the principal meals taken at times when the temperature is not high. Daily spongings with water, or alcohol and water, help, and the hands and arms may

be frequently so bathed. If required, a dose of pyramidon (2–3 gr.) or of cryogenin (3–5 gr.) may be taken a couple of hours before the principal rise, but temperature so controlled must be distinguished from genuine diminution of fever. In the right cases minute doses of tuberculin may bring down a temperature otherwise rebellious; in many cases a mixed infection is responsible for fever, and this must be sought for and in some cases a vaccine tried. The treatment of fever must never be simply symptomatic; the persistently febrile case is a case by itself both for prognosis and treatment.

Cough must be sharply divided into useful and useless. Where useless, and leading to auto-inoculation or disturbance of sleep, it will need some special attention. Often the patient does not realise how much he can control useless cough himself by determined repression, and he must be warned of this. Where, on the other hand, there is expectoration to bring up, efforts must be made to loosen it. Warm spray inhalations, or warm mineral waters or saline drinks will help, or a mixture containing ammonium chloride and some rectified spirit. Cough leading to vomiting may require gastric sedatives containing some opiate if necessary; the clearing of the tubes before meals with the help of warm saline expectorants may help to prevent this. For irritating cough, especially at night, a linctus containing heroin, codeine, (as Heroin $\frac{1}{24}$ gr., or Codeinæ $\frac{1}{8}$ gr., Acid Sulph. Dil. 2 min., Glycerine and Aq. Laurocerasi 10 min. of each, Syrup Tolutani up to 1 dr.), or morphine may be necessary, with careful avoidance of digestive upset. Dry inhalation from a respirator often quiets troublesome cough, such drugs as creosote with menthol, spirits of chloroform or ether being used (as Menthol 1 dr., Creosote 1 dr., Spirit Vini Rect. and Spirit Chloroform $\frac{1}{2}$ oz. of each)—acetone is invaluable in certain cases.

Pain must not be allowed to interfere with sleep and must be treated on general principles. *Night sweats* may be controlled by sponging at bed-time with dilute vinegar or brandy. An open-air régime, the use of porous clothing, and avoidance of too heavy covering do much to check them. Quinine may be tried in some cases, agaricin ($\frac{1}{12}-\frac{1}{8}$ gr.) or an atropine pill ($\frac{1}{200}-\frac{1}{100}$ gr.) is occasionally required for a time. *Indigestion* and *diarrhœa* will be treated on general principles and may necessitate a temporary alteration to a diet which is lighter and either more or less stimulating, according to the nature of the trouble.

Surgical Treatment.—Localised tuberculosis is often near the surface of the body and may call for surgical interference. This, be it noted, can never take the place of other treatment, both general and specific, but bears a similar relation to these as does symptomatic treatment. Surgical measures generally fall under one of three headings.

(a) *Excision of the Tuberculous Area.*—This is less often attempted than formerly; it is now well recognised that excisions can never remove the whole disease, and they should be reserved for cases where all but slight or quiescent disease can be taken away. This is occasionally the case with neck glands; but wide operations are being more and more replaced by conservative treatment.

(b) *Removal of Dead Material.*—This includes attention to bony sequestra, scraping of caseous glands, or their careful removal, often to be accomplished by mere aspiration of soft tuberculous material. Under this heading may come also the necessary efforts to secure adequate drainage in the case of large or deep tuberculous disease, especially where mixed infection is feared or already present.

(c) *Provision of Rest.*—In the case of tuberculosis of joints and mobile parts, rest must be provided to allow repair, and at times to limit auto-inoculation. This necessitates the employment of apparatus of various kinds—splints, jackets, suspension apparatus, weight and pulleys, and a host of other contrivances.

Specific Treatment

Under this heading come all measures directed against the cause of disease—the tubercle bacillus. Chemical poisons analogous to quinine in malaria, emetin in amœbic dysentery, and salvarsan in syphilis we have none, and we require to fall back on the laboratory of the body for the formation of protective or destructive substances. In the case of the tubercle bacillus the nature of these substances is still somewhat obscure. Looked at from the practical point of view specific treatment can be classified according to whether passive or active immunity is aimed at.

Passive Immunity, by the use of a specific serum, is successful in such diseases as diphtheria, where a powerful extracellular poison has to be neutralised, but is of doubtful utility in diseases like tuberculosis, where the poisons are retained in the substance of the bacilli. It is at present uncertain whether the anti-tuberculous serums, such as those of Marmorek, Maragliano or Ruppel exert some slight bactericidal or antitoxic effect, or whether any action they may have is similar to tuberculin, as Wright maintains. Clinical evidence in their favour is highly conflicting and doubtful. Spengler's I. K. claims to possess both passive and also active immunising properties.

Active Immunity, where the human body is required to manufacture its own antibodies, is the road to natural cure, and its judicious

regulation is the basis of rational treatment. Products of the tubercle bacillus, in other words tuberculin, form the stimulus; production of antibodies is the response. The stimulus must not be too great or exhaustion ensues; it must not fall too low or antibodies wane. Judicious treatment will aim at keeping the supply within bounds when excessive (reduction of auto-inoculation) or supplementing it when too low (tuberculin injections). The former of these aims may fail when the disease has progressed too far; it may be impossible to reduce auto-tuberculin to a convenient figure, and the attempt must then be made to neutralise its action. We possess no effective form of anti-tuberculin to inject from without. We must produce it from within, and, fortunately, by skilfully graduated dosage on a good system, such tolerance against the toxin can often be produced that tuberculin no longer exerts its action in doses where formerly it led to over-stimulation and illness.

We thus find that specific treatment concerns itself in the main with three indications, artificial stimulation of antibody formation by tuberculin, control of auto-inoculation, and the production of tolerance.

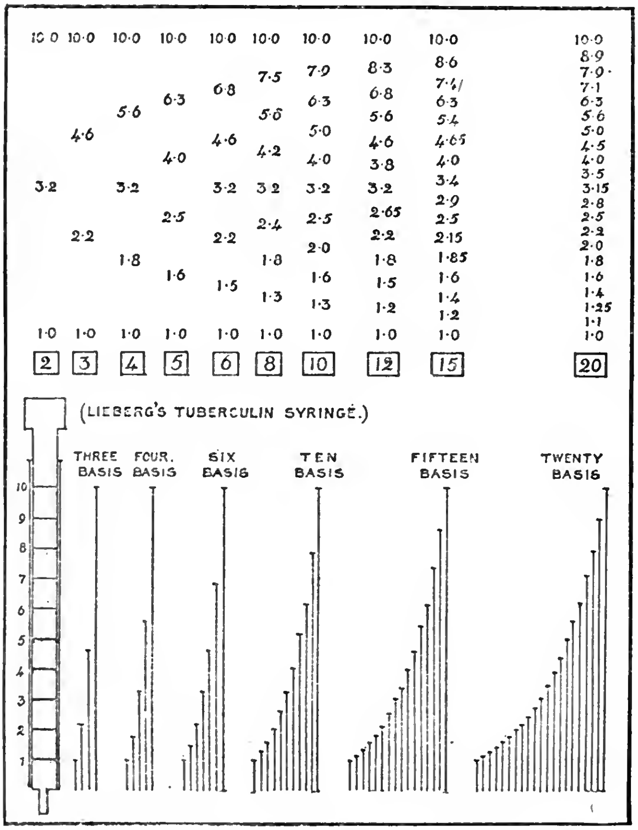
Artificial Stimulation of Antibodies by Tuberculin.—In localised tuberculosis, lupus, dactylitis and the like the supply of tuberculous products (auto-tuberculin) from the lesion may not be sufficient to stimulate production of antibodies and bring about a cure. In these circumstances and also with most forms of chronic and partly healed tubercle, it may be useful or necessary to introduce the stimulus from outside in the form of tuberculin. An efficient therapeutic dose of tuberculin gives rise to the following effects. A "reaction" occurs consisting of three parts: *local*—redness and swelling at the site of injection; *general*—fever, headache, malaise, etc.; and *focal*—congestion in the area of disease. This latter is of value in flooding poorly nourished areas of disease with blood. Accompanying the "reaction" is a temporary lowering of antibody content in the blood as exemplified by its opsonic power. After a day or two all these effects pass off and the patient feels well again—often unusually well. Antibodies increase in the blood, giving the "positive phase" of opsonic power, and the area of disease when visible begins to show signs of healing. This "rebound" after the "reaction" lasts some two or three weeks, and thereafter the effect of that dose of tuberculin is finished.

It is now time to give another dose, and this, if well chosen, is followed by the same effects, till by a series of these responses the area of disease in a favourable case is enabled to heal. This is the small-infrequent-dose method advocated by Wright and suitable for all cases of localised tuberculosis. The preparations T.R. or B.E. are especially suitable, the dose varies with the case and must be that which is just effective, and commonly 0·05–0·1 c.mm. (0·00005–0·0001 c.c.) of either preparation suffices for an adult, and a proportionate dose for a child according to its weight. It is well to begin below the average dose and increase it till a slight general disturbance or some hyperæmia at the focus of infection occurs, and to continue this dose till its activity wanes, when it again must be increased. An interval of two weeks between the doses is generally suitable, but it should be lengthened if a reaction occurs, and may be shortened where the dose is ineffectual. The large-frequent-dose method, and the principles governing it, will be described under the heading of *Production of Tolerance*.

Control of Auto-inoculation.—Though it is the production of tuberculin in tuberculous lesions which stimulates the production of antibodies, and so the cure of disease, the process very quickly tends to get out of control in an organ so vascular and mobile as the lung. Then occur the general symptoms associated with established phthisis—wasting, fever, dyspepsia, etc., due partly to the action of tubercle products—auto-tuberculin—and partly no doubt to poisons produced by the destruction of the body cells. These poisons pass from the foci of disease into the blood, and it is this process we speak of as auto-inoculation. Where the disease is considerable the supply is ceaseless, but with more moderate disease such auto-inoculation may only occur when the focus is submitted to increased vascularity. Such an increase especially follows increased function, and the control of auto-inoculation demands the reduction of function of the diseased organ to its lowest denomination. In the case of the lung all muscular movements, and even mental and emotional activity, increase its function, and control of auto-inoculation must be sought through complete bodily rest. The effectiveness of this control is best tested by temperature and pulse, and the amount of rest necessary to get rid of symptoms varies (see *Rest and Exercise*). In some cases a week's rest, or partial rest, in bed will suffice to abolish fever. In others "typhoid rest" over a long period with careful control of cough (see *Cough*) may be required. In cases where the disease has reached a certain stage of progress all measures may fail to eliminate the symptoms of toxæmia. In certain of these patients it may happen that the disease has remained to a very large extent one-sided; when this is the case, if toxæmia cannot be otherwise reduced the production of an artificial pneumothorax (collapse-therapy) may work wonders. It puts the diseased lung

at rest and thereby reduces absorption of auto-tuberculin, and at the same time favours conditions of repair. Where pleural adhesions render the production of a pneumothorax impossible, an extrapleural thoracoplasty, with removal of ribs, may be made to serve the same purpose in the same class of case carefully chosen.

It might be argued that all the effects of this control of auto-inoculation are likely to be undone as soon as the patient gets up again, and so they will, unless care is taken. The patient is now at the starting-point on the road to tolerance, just as we may bring a case of failing heart on the road to full compensation, or one of neurasthenia, at the end of a rest cure, on the way to full nervous stability. In each case the secret of final success lies in the "graduation" of the succeeding march—the upgrade must not be steeper than the maimed organ can cope with (see also *Rest and Exercise*).



Dosage in Geometric Progression (from *Tuberculin Treatment*, by Riviere and Morland)

The enclosed numeral denotes the "Basis" or number of doses to be given in each Dilution of Tuberculin before passing on to the next. A sensitive case is put on a high Basis—say [15], a tolerant case on a low—say [8]. In any series, every dose is the same multiple of the preceding one whereby all "cliffs" in dosage are entirely avoided.

Production of Tolerance.—Tolerance may be achieved either to tuberculin or to auto-tuberculin, and the former is probably the easier method to follow. With the patient still at rest we begin tuberculin in minute doses and rise by geometric progression, each dose being the same multiple of the previous one (see table), so that no sudden increase of dose may disturb the progressive compensation. By these means we are able to reach without much difficulty quantities of tuberculin a million or more times larger than that with which we started. We thus build up tolerance against both tuberculin and auto-tuberculin, in this way greatly ameliorating the symptoms of auto-inoculation. We are also able by well-arranged dosage to stimulate antibody formation and cause mild focal hyperæmia by each injection, and thus to use tuberculin as a remedy while saving the patient from the effects of its excess. This is the large-frequent-dose method suitable for all cases of autotoxic disease and especially phthisis.

It may be wondered how we are able thus to increase the dose of tuberculin, but the explanation is simple. Every dose of tuberculin is followed by a period of tolerance to reinjection. After a couple of weeks this tolerance has waned, but if the next injection follows in two or three days an increase of dose is needed to insure the same effect, and so larger and larger doses are given about twice a week without more immediate effect than equal small doses given at two or three weeks' interval. The value of this tolerance may be shown as well against auto-tuberculin as against tuberculin. A resting phthisical patient gets fever on rising, but if only one or two doses of tuberculin are given during rest and the patient gets up on the second day after a dose (*i. e.* in the phase of tolerance) there may be no return of fever. Since all cases of phthisis are subject to auto-inoculation from their lesions the intensive system of dosage described above is suitable to this disease.

Practical Points.—It is necessary to begin well below the reaction limit—a dose of 0·001 or 0·002 c.mm. (0·000001 c.c. or 0·000002 c.c.) of any tuberculin is convenient—and the dose may be doubled till some sign of reaction appears. This may be shown by slight local reaction, by a "flattening" of the temperature, or a slight general reaction, symptomatic or febrile. When this point is reached progression must be slow and regular on a basis of about eight to twelve doses in each dilution of tuberculin (see chart) according to the type of case.

The dilutions are made up each one-tenth strength of the next above. Thus dilution I consists of 1 c.c. of tuberculin made up to 10 c.c. with diluent (conveniently normal saline with 0·5 per cent. phenol); Dil. II is 1 c.c. of Dil. I (or one-tenth c.c. of tuberculin original solution) made up to 10 c.c. with diluent, and so on.

Thus—

1 c.c. of Dil. I	contains	100 c.mm.	(0·1 c.c.)	Tuberculin.
1 c.c. of Dil. II	,,	10 c.mm.	(0·01 c.c.)	,,
1 c.c. of Dil. III	,,	1 c.mm.	(0·001 c.c.)	,,
1 c.c. of Dil. IV	,,	0·1 c.mm.	(0·0001 c.c.)	,,
1 c.c. of Dil. V	,,	0·01 c.mm.	(0·00001 c.c.)	,,

And thus one-tenth c.c. of Dil. V contains 0·001 c.mm. (0·000001 c.c.) of tuberculin, the amount recommended for an average initial dose.

If only a local reaction occurs, the same dose is repeated till this wanes; if a general reaction occurs, and especially if focal symptoms, such as increased cough and expectoration are noted, rest in bed is required and the dose withheld until the temperature settles again. The next dose must be reduced $\frac{1}{2}-\frac{1}{10}$ according to the amount of reaction and the length of the interval for recovery. Where the local reaction is properly followed as a guide and no increase of dose made while it recurs, the course can often be completed without any general or focal reaction.

Recapitulation and Conclusion. *Localised Tuberculosis*, in its treatment demands attention to the following principles—

(a) *Hygienic-dietetic Treatment* or general health-building on the lines already laid down save that the difficulties arising from auto-inoculation are absent. On this account open-air and home treatment throughout is more often feasible, though climatic conditions and removal from towns is needed in certain cases.

(b) *Stimulation of the Defensive Mechanism* is especially needed in localised tuberculosis, since the supply of tubercle products from the area of disease is small. Tuberculin should be given on the small-infrequent-dose method.

(c) *Surgical Treatment.*—Removal of dead material—caseous material, hard or soft, bone, etc.—is occasionally required, establishment of free drainage where mixed infections are suspected or manifest, control of movement, and avoidance of deformity by apparatus. A second vaccine to combat mixed infection is occasionally required.

Autotoxic Tuberculosis, of which phthisis is the common example. Cases may be conveniently divided into three classes—

Class (a). *Resting Febrile* wherein auto-inoculation is excessive even at rest. Here the measures advised under "control" of auto-inoculation must be pursued with the hope of bringing the patient into class (b). These are cases for the sanatorium and the specialist, or are beyond the reach of all but palliative treatment. Not infrequently a mixed infection is responsible for their condition.

Class (b). *Resting Afebrile — Ambulant Febrile.* Where symptoms, such as fever, only appear on increased function. Here the indication is gradually to raise their tolerance, till they can be brought into class (c). For this skilled hygienic and specific treatment are necessary, and a course of sanatorium treatment is required at the outset, though the later stages in a favourable case can often be carried through successfully in the home.

Class (c). *Ambulant Afebrile.* — Where patients can go about without any symptoms attributable to auto-inoculation. These cases are especially suitable for home treatment—where means of ensuring hygienic-dietetic, and if possible specific treatment, are available. Often a considerable amount of quiet outdoor exercise and pursuits can be arranged with advantage, but always to the avoidance of fatigue and loss of weight, and also of violent movements which might cause injury to healing parts. C. R.

BACILLARY DYSENTERY

The treatment as regards rest and food is much the same as described under Amœbic Dysentery, except that brandy and opium are more likely to be needed. Bismuth and intestinal irrigation are also useful. Emetine has been found to be of no value in unmixed cases of bacillary dysentery, except perhaps for diagnosis.

Severe cases should be treated as early as possible by serum, or, if that is impossible, by salines, the rule being that the saline is given every hour until the motions become fæculent, and this is repeated daily for three days.

If the exact etiology is unknown, or if it is impossible to prepare an autogenous vaccine, a polyvalent serum, such as Shiga's, may be used.

In mild cases one injection of 10 c.c. into the skin about three inches below the clavicle may be enough to banish blood, mucus and tenesmus, so that the patient gets refreshing sleep. If not, repeat the dose in six to ten hours.

A bad case must have a similar dose twice daily for two or three consecutive days. The injection is to be subcutaneous, not intramuscular. The dose issued by the Lister and Pasteur Institutes is 20 c.c. Urticarial eruptions or pains in the joints, due to the serum, may require lactate or chloride of calcium, 15–30 gr.

For collapse, the subcutaneous injection of normal saline solution is useful.

Very severe cases, which are suspected to involve the whole of the large intestine, and gangrenous cases, may be treated by appendicostomy, which enables the whole large bowel to be washed out with a weak permanganate or boracic acid solution (1 in 160), or, if necessary, with collargol (1 in 500). F. M. S.

LEPROSY

No specific treatment has yet been found, but the recent discoveries showing that the bacillus of leprosy can be cultivated as a streptothrix, or as a bacillus, lead one to hope that some day a reliable vaccine may be produced.

Tuberculin was tried by some of us, at Koch's instigation, in 1890, and often since, but it cannot be recommended. Most drugs are useless unless they improve the general health of the patient. Chaulmoogra oil has apparently cured or arrested the disease, but it has often failed. If the stomach will tolerate it, give it in gradually increasing doses from 20–300 min. daily, either in capsules or in an emulsion with gum. Or it may be given in milk *per rectum*, and it may also be rubbed into the skin of the whole body twice daily. Patients take it best intra-muscularly, but this requires its administration from sterilised tubes, and painful lumps and skin eruptions occasionally occur in spite of attempted asepsis. I once published a temporarily successful result after five years' perseverance, but most patients will not continue any one treatment for years.

Nastin, a crystallisable neutral fat, prepared by Deycke from a streptothrix, and then combined with benzoyl chloride, has been on trial intra-muscularly since 1904; the results are, on the whole, disappointing.

X-rays have been found useful by Heiser in a few recent cases occurring in young, otherwise healthy subjects.

As regards drug treatment, Pasteur's ironical precept must be remembered: "Always hasten to take a remedy while it still has the power of curing!"

Surgical and ophthalmic treatment must be on general lines, as if the patient were not a leper. Tracheotomy is not often required, but it will prolong life when the larynx is invaded and dyspnœa has resulted.

Sulphur baths as an alleviation have been successfully used at Koussatz in Japan and in Egypt.

As regards general measures, the leper may be wise to leave the country in which he became infected, and he should lead the outdoor life of the converted consumptive, and wear specially warm clothing, because the involvement of his skin throws additional work upon his kidneys.

Prevention.—Leprosy in any country ought to be a notifiable complaint. Lepers with open sores, or any nasal discharge, should be isolated until the disease is arrested. The healthy children of lepers should be separated from their parents as soon as possible, and should then be kept under observation. Antiseptic precautions after handling lepers are necessary. There is no evidence that leprosy is due to the eating of any particular food such as fish.

F. M. S.

THE MYCOTIC INFECTIONS

In dealing with the therapeutics of mycotic infections it will be convenient to divide these diseases into three groups: (1) those in which the fungus invades the hair; (2) those in which it attacks the superficial layers of the glabrous skin or the nails; and (3) those in which there is invasion of the deeper parts of the skin, of the tissues beneath, or of the internal organs. Corresponding with these three groups there are three main forms of treatment: (1) when the hair is attacked, depilation (especially by X-rays); (2) the employment of local parasiticides when the infection is superficial; and (3) the administration of potassium iodide for the deeper infections. The reason for the employment of these different forms of treatment in the different circumstances will be presently explained.

1. **Mycotic infections of the hair** include the several varieties of *Tinea Tonsurans* and of *Tinea Barbæ*, and *Favus* of the scalp. Formerly in the treatment of these diseases, ineffectual attempts were made to kill the fungus by means of parasiticides. The multiplicity of the remedies employed is evidence of the ill success of such measures, for, owing to the depth to which the fungus extends in the hair, it is impossible that these applications should reach it. The more rational method is to remove the hair and with it the fungus. This cannot be done by epilation because the infected hair breaks away. Occasionally, by the older methods, one may succeed in attaining this object by the production of inflammation of the affected areas and consequent loosening and fall of the hair; but with the stronger remedies, such as glacial acetic acid, or croton oil, there is danger of permanent baldness of the parts inflamed; and the milder applications cannot be relied upon to produce an inflammation at will. Among the most efficacious are tincture of iodine (or Liq. Iodii fort used with care), Ung. Hydrarg. Nitratis, B.P., and an ointment of equal parts of common salt and vaseline. Repeated applications of either of these remedies will in a small proportion of cases, probably about 1 in 15, lead

to inflammation of the affected areas and consequent fall of the infected hair, with ultimate cure in the course of two or three months. But by far the most rapid and certain method of treating Ringworm of the scalp is by means of X-rays.

The X-ray Treatment of Ringworm of the scalp consists in applying to the affected areas of the scalp, or to the whole scalp, if the disease is at all extensive, measured doses of X-rays sufficient to cause depilation without danger to the skin. If there be only one to three patches of ringworm, each patch may be treated separately by exposure through a circular hole cut in a sheet of lead, and large enough to include a good margin of healthy hair; or a lead-glass cylindrical localiser may be used. When there are more than three patches it is generally advisable to depilate the whole scalp. This is done most conveniently by the "five-exposure" or "Kienboch-Adamson" method. By this method the forepart of the scalp, the crown, the occiput and the sides of the head each receive in turn a single Sabouraud pastille dose of X-rays. In order that there may be an even radiation of the whole scalp, it is necessary to aim the five doses at five equidistant points, and these points are to be carefully marked on the clipped or shaven scalp with a blue skin-pencil. The first point is in the middle line, an inch or two behind the anterior margin of the scalp. Five inches are measured backwards from this point to mark the second point on the crown, and again five inches for the point on the occiput. The two lateral points are marked just above each ear so that they are five inches from each of the three central points. The applications are best made with the patient lying down. The X-ray tube is enclosed in a lead-lined box-shield which has a circular aperture of three to four inches in diameter through which the rays pass towards the scalp. Around the aperture there are fixed three slender converging wooden pegs, the ends of which rest on the scalp and keep the shield and the contained tube at a fixed distance from the skin. The box must be so arranged that the blue-pencil mark on the scalp is exactly in the middle of the points of the three pegs. The anticathode of the X-ray tube should be 6½ inches from the skin, and the Sabouraud pastille exactly midway between the skin and the scalp. The five exposures are given at one "sitting," and the whole procedure occupies from an hour and a quarter to two hours. After the exposures no visible change occurs until the beginning of the third week. During the third week after the treatment the hair falls, both healthy and diseased. The fungus is not destroyed, but merely comes away with the hair upon which it feeds. For six weeks or longer the parts which were exposed to the rays remain absolutely bald, and then the new and healthy hair begins to grow. In the course of a few weeks it may be an inch or so long. A mild antiseptic ointment (Ung. Hydrarg. Amm. Chlor. dil.) or a lotion (Tinct. Iodii 1 oz., Spirit vini methyl 7 oz.) is applied to the whole scalp daily during the treatment in order to disinfect the skin itself. The child is free from infection so soon as the hair has completely fallen. The sole danger of the X-ray treatment is permanent loss of hair from an over-dose. But with modern methods the risk of such a serious occurrence, though perhaps not entirely eliminated even in skilled hands, is reduced to a minimum.

Favus of the Scalp is treated by X-rays in the same manner as ringworm.

Ringworm of the Beard is in many instances of animal origin and, as is characteristic of animal ringworms, spontaneously inflammatory. Depilation then occurs, in course of time, as a natural process, and the only treatment required is that of local antiseptics. One of the most useful is an ointment of oleate of mercury 5 per cent., with resorcin 15 gr. ad. 1 oz. The less inflammatory forms of beard ringworm are generally more quickly cured by X-ray treatment, though on account of the somewhat more difficult technique owing to the irregular shape of the chin, it is advisable first to try treatment by the ointment recommended.

2. **Mycotic Infections of the Glabrous Skin** include Tinea circinata, Tinea cruris, Eczematoid ringworm of the fingers and toes, Favus of animal origin and Tinea versicolor. These eruptions are for the most part readily cured by the application of local parasiticides, and there is no indication for X-ray treatment. *Tinea circinata* (or ringworm of the body) occurs in the form of scaly rings or patches in association with scalp ringworm, or it may be derived from the cat or the dog, in which case the rings are more inflammatory and often vesicular. Still more inflammatory and pustulating eruptions result from infections from horses or cattle. In all forms of Tinea circinata the local application of tincture of iodine is a favourite and an efficacious remedy, although it has the disadvantage of producing exfoliation or crusting, and may thus render it difficult to know when the disease is cured. For the pustulating ringworms there is no better treatment than a daily application of tincture of iodine. In the less inflammatory forms the ointment of nitrate of mercury is a well-tried and useful remedy, but the ointment containing benzoic acid, as recommended below for Tinea cruris, is probably better than any other application. *Tinea cruris* or ringworm of the groin (formerly called Eczema marginatum and known in India as Dhobie Itch) is usually regarded as an

obstinate complaint. The older treatments by application of iodine or by use of chrysarobin ointment (Goa powder of India) are objectionable on account of the local inflammation which they often produce in these parts where the skin is tender. They may now be discarded for a cleanly and rapidly efficacious ointment which we owe to Dr. Arthur Whitfield, as follows—

℞ Acid Salicylic gr. x-xv
Acidi Benzoici gr x-xv
Ol. Coca-Nucis ʒ vi
Vaselin ad. ℥ i

Eczematoid Ringworm of the Toes and Fingers.—Many so-called eczemas of these parts are really ringworm, and often associated with ringworm of the groin (Eczema marginatum). They are easily cured by benzoic acid ointment. *Pityriasis versicolor*, or Tinea versicolor, is a macular eruption of the chest and back due to a fungus (microsporon furfur) and seen often in phthisical persons, or those who sweat much and wear flannel. It may be cured by the frequent application of sulphurous acid, 1 dr. in 1 oz. of water.

Favus of the Glabrous Skin is occasionally met with in this country, at any rate in London, as a result of contagion from a mouse or a cat infected with favus. It occurs as red scaly, or vesicular, or crusted circles or rounded patches like those of ringworm of the body, but distinguished from the latter by the presence of one or more sulphur yellow favus cups or sculuta. The eruption is cured by removal of the sculutæ, and application of a local antiseptic, such as iodine or mercury.

Ringworm or Favus of the nail is best treated by covering the affected nails with a wad of wool soaked in tincture of iodine under a finger-stall. The cure takes several months. X-ray treatment or evulsion of the nail is usually unsuccessful.

3. **Mycotic infections of the deeper parts of the Skin, of the Tissues beneath and of the Internal Organs.**—These include actinomycosis and other forms of streptothrix infection, and the more recently discovered sporotrichosis and blastomycosis. The features of actinomycosis are described in all the text-books, and need not be recalled here. In *sporotrichosis* there occur gummatous lesions in the skin, sometimes in the muscles and bones, and very often in the viscera. They suggest those of syphilis or of tubercle, but yield cultures of a fungus called sporotrichum. The disease is fairly common in America, both North and South, and on the continent, especially in France, but a few cases only have as yet been discovered in this country. *Blastomycosis* is a disease due to a yeast fungus which manifests itself chiefly as local, fungating ulcers of the skin, but which may become a systemic infection. Most of the cases recorded have occurred in America. In both these affections, but particularly in sporotrichosis, the internal administration of potassium iodide in large doses (up to 60 gr. daily) may lead to a complete cure. Actinomycosis may also be cured by iodide of potassium, unless the disease is very extensive and accompanied by secondary coccic infection. In actinomycosis surgical treatment of total extirpation or of scraping, combined with local antiseptics, may also be employed. Surgical treatment in sporotrichosis or in blastomycosis is inadvisable. The action of iodide of potassium in sporotrichosis has been carefully studied by de Beurmann and Gongerot, who have shown that it produces its effect, not as a direct parasiticide, but as a stimulant of phagocytosis. These observers think it possible, however, that a bactericidal nascent iodine is also disengaged by the action of the living cells. Serum and vaccine treatments have been employed in these deep-seated mycotic infections, but hitherto the results obtained have been less successful than those from potassium iodide administration. H. G. A.

DISEASES DUE TO PROTOZOA

AMŒBIC DYSENTERY

Whether the case is acute or sub-acute, as usually seen out of Great Britain, or whether treatment is required for symptoms occurring in a case imported from abroad, *rest in bed* for at least a week is an essential which will do much to assist the cure.

A flannel belt or broad bandage should be worn by day and night, and for severe pain fomentations are necessary.

Rest is all-essential for the ulcerated intestines, so that in very severe cases the diet must be restricted to albumen water, rice water and whey. Brandy should not be given unless it is absolutely necessary.

In ordinary cases milk boiled, sterilised or peptonised, may be given diluted with rice water. Those who think they cannot drink milk may require the addition of sodium citrate, 5 gr. to each feed.

Every two hours a feed of about 4 ounces should be drunk very slowly, and it must be neither hot nor cold.

Soup and meat extracts are better avoided until the number of motions is lessened, when arrowroot, Benger's food, eggs and milk puddings may be cautiously added. Then soft food such as rusks, pounded fish, chicken and bananas, and, later, toast, chicken, pigeon, followed, in the fulness of time, by meat, vegetables and fruit.

A daily inspection of the fæces must determine the menu. Thirst may be relieved by allowing the patient to sip a simple acid lemonade or a solution of lactic acid (1 in 3000).

The preliminary general treatment is not unlike that of enteric fever, and the fæces must be disinfected or burnt and protected from flies, with equal care.

Drugs.—An initial aperient is necessary to get rid of the relics of previous improper diet, and it is surprising to find how much fæces are retained, even when twenty to thirty motions are being passed in the twenty-four hours. One dose of castor oil may be given, or drachm doses of sulphate of magnesium (with Tinct. Card. Co.), or from four to six doses of calomel, $\frac{1}{8}$ gr. with Sod. Bicarb., 3 grs. every hour.

Intra-cellular (not subcutaneous) injections of emetine hydrochloride should be given without delay; $\frac{1}{2}$ gr. once a day, increased, if necessary, to $\frac{1}{2}$ gr. twice a day. This valuable remedy, re-introduced in 1912 by Leonard Rogers, causes no depression, nausea nor vomiting, and is now being so much used that its market price has doubled since September 1912. The patient will probably experience slight tenderness at the site of injection on the succeeding day.

To try to obviate the cost of emetine, a rival preparation, amebetine, has been produced, which contains emetine unseparated from cephæline, another alkaloid of ipecacuanha; the dosage is similar to that of emetine.

Emetine can also be administered by the mouth if the drug is sufficiently coated by keratin.

Emetine treatment should be continued for at least two weeks, and may have to be re-commenced if amœbic cysts are found later in the fæces.

Tenesmus can be checked by small enemata of saline solution or by suppositories of cocaine, opium or belladonna. Hæmorrhage from the bowels must be treated by an ice bag on the abdomen, opium, calcium lactate or digitalis by the mouth, or enemata of iced water.

If the fever accompanying the dysentery is thought to be malarial, quinine must be given.

As soon as convenient, it is well to put the patient on bismuth, preferably the salicylate, 15 to 30 gr. every four hours, and to continue this for at least two months.

The treatment should be prolonged after all symptoms have disappeared to prevent possible relapses and development of liver abscess.

Obstinate chronic cases, which do not yield to two different courses of emetine, prolonged bismuth and careful rest and dieting, may be benefited by Plombières treatment, as carried out in France or at Harrogate or in London.

Former Treatments.—1. If no emetine can be procured, recourse must be had to the best Brazilian ipecacuanha, which was introduced into England as a cure for dysentery late in the seventeenth century. The following method was employed at the hospital connected with the London School of Tropical Medicine in the pre-emetine days. The patient must be starved for four hours, a mustard plaster is applied to the epigastrium, and the patient is made to lie flat in bed without any pillows. Fifteen min. of laudanum in water are then given, and after a quarter of an hour 30 grs. of ipecacuanha powder. To prevent vomiting, the patient is kept rigidly at rest, the nurse, sitting by his side, is ordered to wipe away saliva to avoid his making any movement, and no food is given for at least three hours after the dose. On the next night the same treatment is carried out, except that the ipecacuanha is reduced to 25 gr. and the laudanum to 10 min. On the third night the ipecacuanha consists only of 20 gr., preceded by 5 min. of laudanum. On the fourth night laudanum is discontinued altogether, and the ipecacuanha is further reduced to 15 gr. On the fifth night, 10 gr., and on the sixth night, 5 gr. of the drug are given. The treatment is then continued with a nightly dose of 5 gr. for another week or ten days. In spite of the vomiting and the annoyance of having to lie absolutely still, this treatment has proved to be most useful, and the amœbæ are found to disappear from the stools after the second or third dose. In order to lessen the risk of vomiting, the ipecacuanha may be administered in "membroids," or in stearin-coated pills.

2. Saline treatment every day by drachm doses of sulphate of magnesium with or without sulphate of soda, succeeds when ipecacuanha fails; it has been thoroughly well tried since 1877, when Bartholow of Ohio introduced it.

3. When acute symptoms are arrested, intestinal irrigation is often useful once or twice a day, the drugs used being, of course, those which will kill the amœbæ *in vitro*, e. g. quinine 1 in 5000, increased to 1 in 500, nitrate of silver, 1 in 1000, or sulphate of copper, 1 in 1000.

Whichever drug is employed the routine method is the same. A long tube and funnel, or a reservoir containing 3 pints, are indispensable. The rectal tube must be at least 3 feet in length and soft enough to avoid injuring the bowel; after being well greased, with boric vaseline, it should be introduced, if possible, its whole length. The fluid is not injected, but allowed to run in slowly during some minutes. The patient should assume the knee-elbow position, or else the buttocks must be raised on pillows, and the foot of the bed elevated on blocks. If the anus be very sore

from many acrid discharges, it may be painted with cocaine before the operation, or a suppository of one grain of cocaine may be inserted half an hour before the irrigation. Until the patient becomes accustomed to the treatment the tube should be passed by the medical attendant himself. All adult patients can hold one pint, rapidly increased to 2 pints, and some can gradually accustom themselves to take 4 pints or more. The enema need not be retained more than five minutes, and need never be given more than twice a day. As a rule, an enema of this kind every morning is enough, and in the evening a simple cleansing enema, such as 2 pints of saline solution, or water in which 1 ounce of linseed has been allowed to soak for some hours. This soothing enema may be retained by the patient as long as he likes. All enemas must be given warm.

It is obvious that any drug used is absorbed to some extent, for I have seen temporary poisoning after large enemata of boracic acid, starch and water, and similar cases have been recorded.

Sceptics who do not believe that the irrigation gets beyond the rectum may need to be reminded that bismuth, introduced by enema, has been seen by X-rays to have reached the cæcum.

Prevention.—Water and milk must be boiled, salads and uncooked vegetables eschewed, and butter and ice considered suspect, while food must be guarded from flies, dust, excreta and doubtfully clean hands. Children and young people should be specially protected by suitable clothing, regulated diet and avoidance of fatigue.

F. M. S.

SLEEPING SICKNESS

We have no specific drug for sleeping sickness, such as quinine in malaria, mercury in syphilis and salvarsan in yaws, yet there are several remedies in use which greatly benefit or even cure the condition. In the early days arsenic in the form of liquor arsenicalis was used, and it is of interest to note that at least two of the cases so treated recovered. Later the arsanilates, atoxyl and soamin, were introduced and better results were obtained with them, but unfortunately when used in large doses over prolonged periods of time, optic neuritis is apt to develop. Arsenophenylglycin, an organic arsenical compound discovered by Ehrlich, various benzidine dyes, antimonial salts, mercury salts in combination with atoxyl, and more recently salvarsan, have also been tried.

The antimony treatment has apparently succeeded in several cases and has been fairly extensively tried by Sir Patrick Manson at the London School of Tropical Medicine.

Dr. Newham, the director of that institution, has very kindly supplied me with the details of the method, these being as follows: The salt used is the *Antimonium Tartaratum*—potassio-tartrate of antimony or tartar emetic—the dose employed being from $\frac{1}{2}$–$1\frac{1}{2}$ gr. This is carefully weighed out and added to 4 oz. of normal saline in a glass flask, the neck of which is then plugged with cotton-wool. After this the flask is boiled for ten minutes over a bunsen burner, this completing the solution of the drug and also sterilising the mixture. A second flask containing 10 oz. of normal saline is also prepared and sterilised at the same time. The apparatus for the injection consists of a yard of soft rubber tubing ($\frac{3}{16}$ in. bore). A small glass funnel is inserted into one end of this while a fine silver canula fitted with a stop-cock is attached to the other. Sterilise carefully. Next select a superficial vein in the leg or arm. Sterilise the skin over this by painting with tincture of iodine and inject a little novocain near the point to be opened. Dissect out the vein for half an inch and apply two ligatures at either end of this. Tie the distal one, leaving the ends long for the purpose of holding and steadying the vein. An opening is then made above this and the canula of the injection apparatus, which is filled with normal saline heated to a temperature of 102° F., is inserted, the proximal ligature being tightened around it to keep it in position.

An ounce or two of normal saline is then allowed to run slowly into the vein, and if the flow is satisfactory and no leakage is taking place the tartar emetic solution, also heated to 102° F., is poured into the funnel and gradually allowed to enter. The rate of flow is controlled by means of the stop-cock on the canula, or by raising or depressing the funnel, and should not exceed 1 oz. of fluid per minute. When most of the tartar emetic has run in and only a small amount remains in the funnel, some 3 oz. more of the normal saline solution are added so as to wash out completely all the antimony solution into the vein. When only a little of this is left, turn off the stop-cock and slowly withdraw the canula from the vein. Before this is completed an assistant ties the proximal ligature as soon as the point of the canula has passed the spot where it (the ligature) encircles the vein, thus completely occluding the vessel and preventing the ingress of air. The ends of the ligatures are then cut short, the wound is closed by a suture, and suitable dressings are applied.

Throughout the operation great care must be taken that the funnel is never allowed to become empty of fluid, otherwise air will enter the vein.

Also the tartar emetic solution must on no account be allowed to escape into the tissues, otherwise an extremely painful necrosis is sure to follow. Provided the solution is run in slowly and the dose has not been too large, no special symptoms are produced by the injection, but in some instances a paroxysmal cough appears and a feeling of oppression in the chest is complained of. Alarming symptoms, twenty minutes or so after the injection, have been recorded, namely, severe rigor, high temperature, vomiting and collapse.

When atoxyl is given it must be administered intravenously or intramuscularly. Todd, of the Liverpool School of Tropical Medicine, recommends the following procedure: Make a 20 per cent. solution of atoxyl in normal saline, warm to blood heat before using, and inject the following doses: 0·6 c.c. every day for four to six days, then raise to 0·8 c.c. for another four to six days, then again raise the amount to 1 c.c. per day. Continue to give this dose until signs of intoxication begin to appear. When this happens, reduce it, as in the ordinary administration of arsenic, until the limit of the patient's toleration is reached, and keep the dose at that point.

As already stated, the danger of giving excessive doses of atoxyl lies in the production of optic atrophy, leading to total blindness. Smaller doses (3 gr. or so) alternating with antimony and other drugs are still given by some, and undoubtedly prove useful.

Broden, Rodhain and Corin have recently given salvarsan an extended trial in the treatment of sleeping sickness cases in the Congo. Doses of 0·4 and 0·6 gm. were given intravenously. These observers conclude that the drug has a rapid and energetic action on the trypanosome, and that it also has a beneficial action on the patient. Further trials should, therefore, be given to it.

Whichever line of drug treatment is adopted, it must be clearly understood that the fight for mastery over the trypanosome will be a long one. Such being the case, it is all important to build up the patient's strength in every way by good food and good hygiene, so as to prepare him for the struggle. Chills must be very carefully avoided, intestinal parasites if present must be expelled, malaria and syphilis, if present, suitably treated, and every effort made to avoid over-exertion or anything that may cause debility. G. C. L.

KALA-AZAR

The treatment of this common and important Eastern disease cannot be said to be satisfactory. The mortality due to it has been variously estimated from 75 per cent., after long courses of quinine (Price), to 98 per cent. in untreated cases or in cases treated by other methods.

Rogers in India has recommended, and still recommends, large doses of quinine, 60 gr. or even 90 gr. a day being given for considerable periods of time. These doses, though in some instances distressing to the patients, often change the high remittent types of fever seen in this disease into harmless low intermittent ones and otherwise ameliorate the symptoms. A certain percentage are said to recover. Castellani and Chalmers also believe that the best method of treatment is by the administration of quinine in massive doses, supplemented by a course of quinine cacodylate injections or atoxyl injections. One of their patients apparently recovered on a treatment of quinine sulphate (30 gr.) and euquinine (30 gr.) daily by the mouth, together with a daily intramuscular injection of quinine hydrochloride (15 gr.) alternating with one of quinine cacodylate (4 gr.). Manson, on the other hand, believes that these massive doses of quinine are not only useless but harmful, and certainly in some of the cases I myself have seen at the London School of Tropical Medicine no amelioration of symptoms followed such a line of treatment.

Atoxyl has appeared to do some good in certain cases, Manson having treated four patients with it. In two no improvement followed, but in the others a cure seemed to result. Further trials by other observers have not confirmed the value of the drug, however.

Of other drugs tried one may mention arsenic, methylene blue, cinnamate of soda, senega, trypan red and antimony. Intravenous injections of the latter have been very efficacious in some cases of human trypanosomiasis, and an extended trial should be given to it in kala-azar. Salvarsan is also certain to be tried, but as the disease is in no way related to spirochætal maladies the efficacy of this drug will probably be nil. Rogers treated three cases with staphylococcus vaccine, and they recovered, but as they had also been treated with large doses of quinine it is uncertain to which of the remedies, if either, one must attribute the success. Vaccines prepared from the Leishman Donovan parasites themselves are still *sub judice*. X-rays have also been tried, but have failed. Occasionally, remarkable spontaneous recoveries from an apparently hopeless state take place, and, as Rogers says, much caution is required in making deductions regarding any line of treatment—such recoveries, however, encourage the hope of the ultimate finding of a curative drug.

The rest of the treatment must be purely symptomatic. Any parasitic worms present

should be got rid of. The patients should have good food and be kept in the best of hygienic conditions.

Hæmorrhages are often troublesome. For these calcium chloride may be tried. If from the nose, Tinct. Hamamelis (Hazeline) or other styptics will be found useful, or the nares even may have to be plugged.

Diarrhœa is to be controlled by opium and astringents. Ascites, if extensive, will require tapping.

Prophylaxis.—There are good grounds for believing now that the *Leishmania donovani*, the causative parasite of the disease, is transmitted from man to man by the bites of insects. Patton in India incriminates the bug. This insect should be destroyed, therefore, wherever possible, and no one should sleep in houses where kala-azar patients reside or have resided unless certain that they are scrupulously clean and free from bugs. The destruction of old bug-infested coolie lines in Assam and the building of new ones is said to have greatly diminished the disease in these parts.

G. C. L.

MALARIA

Malaria, though known to Hippocrates, was never scientifically studied until after 1639, when cinchona bark was imported into Europe by the Countess of Chincon, wife of a Viceroy of Peru, who had been cured of malaria by it. By means of this drug Charles II was cured of a tertian fever in 1679, but it was not until 1820 that quinine was shown to be the active principle of the bark.

Unless the patient is comatose or otherwise dangerously ill, it is better to postpone the administration of quinine until the diagnosis is firmly established and until it is clear which form of malaria has to be dealt with, and at what hour the paroxysms are likely to occur. It must be borne in mind that if the patient has recently taken quinine it is often impossible to find the parasite in the peripheral blood.

Quinine is the specific drug which is certain to cure malaria, if only the prescriber understands how to use it, but there are three essential points in addition. Bodily rest is important, and quinine is more effective when the patient is confined to bed. Bed should, therefore, be insisted on in cases of sub-tertian infection.

The diet should consist during the fever, and for twenty-four hours after its cessation, of nourishing liquids, but after that the patient may have any ordinary digestible food.

The bowels should be freely opened by small repeated doses of calomel ($\frac{1}{6}$ gr. every hour), as early as convenient; this improves the patient's condition and favours the action of the quinine. For the sake of others, the patient must be protected from mosquitoes.

Choice of Quinine Salt.—There are more than twenty varieties, of which only six need be mentioned here.

1. Sulphate is the oldest and best known. It should never be used for malaria, because it is difficult to digest, requiring 800 parts of cold water to dissolve it. This necessitates the use of a dilute acid with it, which often causes indigestion and constipation, for which the quinine gets the blame.

2. Bisulphate is soluble in eleven parts of water, and is exactly the same price as the sulphate. This is an ideal salt for governments and hospitals.

3. Bihydrochloride is soluble in two parts of water and is the salt invariably used for intra-cellular injections. The objection to this salt is that its price is nearly double that of the bisulphate. It is excellent for private patients.

4. The hydrochloride is preferred by some (soluble 1 in 40 of water) because it is a little cheaper than the bihydrochloride, which they also think is too soluble.

5. Euquinine is better taken by children and some delicate people, but it does not prevent cinchonism. It is seven times more expensive than the bisulphate.

6. The tannate has the advantage of being almost tasteless, and, in a chocolate basis, is well suited for children.

Time of Administration.—When a malarial paroxysm has begun, quinine will not check it and will only make the patient more uncomfortable; it is, therefore, better to wait until the sweating stage, or the fever-free period. By this method the quinine comes into contact with the youngest forms of the parasite, on which it acts most vigorously. Our aim is to give it four hours before the rigor, that is, before the sporulation of the parasite is due. If the hour of the expected rigor is unknown I give quinine in three separate doses, at 6, 8 and 10 a.m. to anticipate the rise of temperature, which is often in the afternoon. The quinine treatment must be continued for at least two months in the mildest cases, and for periods varying from three to six months in severe cases.

Methods of Administration.—1. If there is no vomiting or diarrhœa, it is better to give quinine by the mouth in solution, capsule, cachet or uncoated tablet, for ancient pills and coated tablets sometimes pass through the alimentary canal unabsorbed.

2. Treatment per rectum is unsatisfactory, whether by enema or suppository, because absorption is slow and irritation is caused.

Moreover, 50 per cent. more than by the mouth must be given.

3. The intra-cellular method (not subcutaneous) acts more quickly and does not irritate the stomach. Painful hard lumps are sometimes caused at the site, but careful asepsis prevents the risk of abscesses. The syringe and needle, after being boiled, should be sterilised by carbolic solution, 1 in 20, to counteract any tetanus spores which might be present in the tropics. (See article on *Tetanus*.)

4. Intravenous injections are used when the patient is already comatose and there is great need of hurry, as in pernicious infection with sub-tertian parasites. Fifteen gr. of quinine bihydrochloride should be dissolved in 2 pints of saline solution, and injected slowly with the point of the needle directed towards the heart. The pulse should be carefully noted during the injection.

5. Suckling children can be treated by giving quinine to the mother, or quinine powder can be put directly into a child's mouth, and the mother can give the breast or bottle immediately to prevent unnecessary crying, spluttering and vomiting.

Dosage.—There is only one exception to the rules under this heading. If large, ordinary doses of quinine are given to a resident in a blackwater district, or even to one who has recently returned to Europe from a blackwater district, and if the individual has not recently been taking quinine regularly, an attack of blackwater fever may be produced even in the British Isles. Lest there should be any mistake upon this point, and lest it should colour the erroneous view that quinine is dangerous because it produces hæmoglobinuric fever, I wish to state that it is rather the want of regularity in taking the quinine than the excessive dose of the drug which accounts for the occurrence of this awkward, and sometimes dangerous, complication.

In such cases, instead of giving the ordinary dose at once, it is better, if the patient is not dangerously ill, to re-educate the internal organs to a large dose of quinine. This can be accomplished by beginning with such small doses as 1 gr. three times a day, and gradually increasing during a week to treble that dose, until eventually the ordinary dose can be given without fear. During this period of re-education the urine should be carefully watched and measured, and the patient should be in bed.

Let us now take the case of a malarious individual in whom there is no obvious risk of producing blackwater fever. For an adult less than 5 gr. or more than 30 gr. in the twenty-four hours are useless. It must never be forgotten that quinine is a mild poison, and restraint must be laid upon the evil doer who, to compensate himself for previous neglect of the drug, offers to take unnecessarily large doses, such as 60 gr. This is waste of good quinine and brings legitimate quinine treatment and quinine prophylaxis into disrepute. Ten gr. every two hours up to 30 gr. in each twenty-four hours, continued for two successive days, will, provided it is given after the paroxysm, prevent temporarily the recurrence of tertian and quartan fevers. Then give 5 gr. three times a day for a week, and follow that with 5 gr. daily for three months. With the sub-tertian variety give 5 gr. every four hours on the first day and then continue it every six hours for a week.

If used intracellularly, the periodicity will be broken by injecting 8 gr. every day for three days.

Salvarsan, 0·6 gm. injected, has been successfully tried by others in cases which are said to be refractory to quinine. I have never met a case of malaria which did not yield to quinine properly administered, but I have seen one English lady who suffered from hæmorrhage from the mouth and gums and into the skin after three tonic doses of quinine, each 2 gr. People with this rare idiosyncrasy should, of course, never visit a malarious country. Except salvarsan, which is still on its trial, there is no efficient substitute for quinine in malaria.

Cinchonism can be mitigated by adding Acid Hydrobrom. Dil. 20 min. to each quinine dose, but not by substituting Quin. Hydrobrom.

Symptomatic treatment consists chiefly in giving warm drinks and extra blankets during the cold stage, sponging in the hot stage, and strychnia or camphor when the heart is weak.

Ordinary antipyretics are harmful, but an occasional dose is permissible to secure sleep. Some Europeans still believe that they can cure themselves of malaria by inducing copious sweating. Cachexia requires a good climate, iron, arsenic, Warburg's tincture and fatty food.

Peripheral neuritis, enteritis and other complications will generally yield to prolonged treatment with quinine. When malaria is complicated with pregnancy it is to be remembered that malaria will probably empty the uterus, even if quinine be withheld, and also that large doses of quinine will not act upon a normal gravid uterus.

Prevention.—This is not the place to speak of public measures, but a brief note may be given of personal and domestic prophylaxis.

The "tenderfoot" should be warned of three axioms: 1. To regard his mosquito net as his most valuable possession, unless his house is mosquito-screened with wire gauze. The net must be in perfect repair and arranged outside the poles so that insects outside cannot bite

the sleeper through the net. While travelling the net must not be forgotten.

2. There is a special danger of being bitten between sundown and bedtime, because the insects are then lively and hungry and man is tired and sleepy. If there is no mosquito-screened balcony a wise individual will specially protect his feet and legs, and will not despise anointing himself with citronella or lavender oil.

3. Quinine must never be regarded as a substitute for mosquito screening, but 5 gr. should be taken regularly every day by an adult and half that quantity by a child. If this is not enough a double dose should be taken on Sundays.

Punkahs and electric fans are disliked by mosquitoes. No standing water nor breeding pools must be allowed near the house, and all old tins, bottles and puddles must be banished.

F. M. S.

BLACKWATER FEVER

Bed, warmth, fomentations to the loins, trained nursing and an initial purge of calomel and jalap are essential. If vomiting prevents a powder being retained, a soap and water enema should be given; also ice to suck and small doses of champagne or brandy.

The great thing is to keep the kidneys acting, so the urine must be measured, and the drinks should consist of barley water, albumin water, whey, tea, weak chicken broth and plenty of aerated water. Later, milk, peptonised food and meat juices may be allowed.

If the vomiting continues or the kidneys fail to act, give normal saline solution *per rectum* or subcutaneously or even intravenously. A hypodermic injection of morphia will sometimes relieve the vomiting and the backache. Anuria may require cupping to the loins.

A dose containing Sod. Bicarb. 10 gr., and Liq. Hyd. Perchlor. 30 min. is usually given every two hours for one day and then every three hours until the urine improves in colour.

It is better, if possible, to avoid quinine during the attack and then give it by the educative process described under malaria dosage. The patient should continue to take quinine for at least six months and should convalesce as soon as possible in a non-malarial country.

Prevention.—Rules as for malaria. The patient must be taught before his return to the tropics not to neglect mild attacks of malaria. If he has a second attack of blackwater fever he should not be permitted to return to a malarial country, because it is evident that either he has neglected proper precautions, or he has some special liability to hæmoglobinuria.

F. M. S.

RELAPSING FEVER

Salvarsan is now the specific treatment; 0·2–0·3 gm. injected intravenously causes the temperature to fall to subnormal in seven to fourteen hours, with a disappearance of spirochætes from the blood. As a rule there is no relapse, but if one occurs a second injection may be given.

Deaths have been recorded after a dose of 0·5 gm., so that some authors prefer to use neosalvarsan, which is less toxic. Rectal and intramuscular injections are less satisfactory than intravenous. There is every reason for supposing that this new treatment is equally serviceable for the various types of relapsing fevers in Europe, Asia, Africa and America.

Patients should be given as much fresh air as possible, and an unlimited quantity of water to drink. Salicylates relieve pain in the limbs and head, constipation requires sulphate of magnesia, and during convalescence diarrhœa must be guarded against by not prematurely permitting solid food. Quinine is useless excepting as a much-needed tonic after the fever.

Prevention consists in avoiding native huts and old camping-grounds which harbour the lice, ticks and perhaps bugs, which convey the disease to man. A mosquito net at night protects to some extent from these insects, but care must be exercised in inspecting any bedding which may have been used by natives, or which has been under their care.

Tick Fever. See *Relapsing Fevers.*

F. M. S.

YAWS

Within the last two years (1911–1912) it has been clearly shown that salvarsan or neosalvarsan are specifics in yaws much in the same way as they are in syphilis. Alston in Trinidad, Strong in the Philippines, Castellani and Perry in Ceylon, Cockin in Grenada, Hughes in St. Lucia, West Indies, and Sabella in Tripoli, have all reported marvellous results from its use. Some of these have used the drug intramuscularly, others intravenously, and though the latter is probably the best method of administration, yet the former seems to be quite efficient. Various doses have been tried by the different observers. Sabella, mentioned above, gave an adult male 0·7 gm. of neo-salvarsan intravenously, a woman and a thirteen-year old boy 0·4 gms. The effect of the drug was immediate, the man being cured in fifteen days, the other two patients in shorter periods. Other cases received 0·4–0·5 gm. of neosalvarsan also by the intravenous method. One dose generally effects a complete cure.

Perry in Ceylon treated fifty-four cases, the

doses used for adults varying from 0·3–0·6 gm. of salvarsan, either by the intramuscular or intravenous methods. The results are described as "little short of miraculous," granulomata disappear very rapidly, bone pains quickly vanish and deep tertiary ulcers heal in three weeks or so.

Hughes in St. Lucia advocates 0·6–0·8 gm. of salvarsan to adults and also is enthusiastic about the results obtained. Under old methods of treatment the average duration of stay in hospital was three months; by the new method it is twenty-seven days or less, a saving of over two months. An average dose of salvarsan for an adult may, then, be put down as 0·6 gm. One dose is generally sufficient to bring about a complete cure. If small doses are given originally, relapses may occur, but these can easily be cured by a second injection. In addition to the drug treatment, the patient's health should be improved as much as possible by good food, tonics, fresh air, sea bathing where possible, and mild aperients. Chills are specially to be avoided. Mercury and potassium iodide are now things of the past and need only be mentioned. Ulcerations and sores should be kept clean and dusted with some antiseptic dusting powder. It is astonishing how quickly these heal up after salvarsan. During convalescence an iron arsenic and quinine tonic will be found useful. G. C. L.

SYPHILIS

The present-day treatment of syphilis can be divided into two heads: (1) Local; (2) General.

Local Treatment.—A chancre should be excised when possible; if in a position which contra-indicates excision the sore should be cauterised, or frequently bathed with Lotio Nigra and Unguentum Hydrarg. well rubbed in until every trace of the induration has disappeared. Ung. Hydrarg. should also be rubbed in the skin over any enlarged lymph glands. Condylomata should be frequently bathed with antiseptic lotions, then kept dry with a powder which contains calomel.

℞ Hydrarg. Subchlor. gr. x
Magnes. Carb. gr. xx
Zinci Oxidi
Xeroformi āā gr. x
Pulv. Amyli ad. ℥i
M. f. Pulv.

Rubbing in a mercurial ointment will hasten the disappearance of any syphilitic skin lesion.

The local application of Iodipin with or without Tinct. Bellad., according to the severity of pain, will assist in bringing about the resolution of a periostitis. For joint affections Scott's dressing is the best application. For chronic ulcers cleanliness is the chief point to attend to, and when the ulcer is clean, either the use of a mercurial ointment or the judicious employment of Scarlet Red will assist in the general treatment. It must not be forgotten that any scabs should invariably be removed because their proteolytic action on the tissues underneath may increase the ulceration, although the primary cause has been got rid of. The local application of salvarsan to chronic ulcers on the leg or to the tongue, in chronic glossitis, often affords great relief. A 0·1 gm. ampoule dissolved in ½ oz. water or glycerine should be applied two or three times a day for a few days.

General Treatment.—Three drugs only need be considered, mercury, iodine and arsenic.

Mercury.—The best method of prescribing mercury is in the form of inunctions, but these are useless, except in congenital syphilis, unless carried out by a trained rubber. Mercurial inunctions are messy, and cause the patient some inconvenience, owing to the time they take up. More convenient are mercurial injections. The insoluble preparations are more efficacious than the soluble. The strongest compound is the subchloride, but unfortunately its use is so frequently accompanied by pain and occasional abscess formation that some preparation of metallic mercury is better. The best painless Grey oil is the following (Captain Adam's formula)—

℞ Hydrarg. 20 parts
Anhydrous Lanoline 30 parts
Chlorbutol 2 parts
āā by weight
Liq. Paraffin to 100 by measure
5 ♏ = 1 gr. Hg.
Sig. Inject. 5–10 ♏ weekly.

Injections can be made either into the buttocks or scapular muscles.

The insoluble preparations, of which asurol is the best, are now seldom called for owing to the rapid action of salvarsan, but if this is contra-indicated and the symptoms are such that the patient should be got under the influence of mercury as soon as possible, daily injections of 1 c.c. 5 per cent. Asurol sol. (= ·02 gm. Hg.) or Enesol (salicylarsenate of mercury) should be given. Injections every other day of 0·025–0·10 gm. of Antiluetin, an antimony salt, can be prescribed as an alternative if required.

When a patient cannot get regular medical attendance, mercury should be taken internally in some form; if this method causes depression or sets up gastro-enteritis or diarrhœa, a suppository of 1 gr. of mercury salicylate in Oleum Theobromi ½ gr. inserted every night just before going to bed will often meet the difficulty.

For use in the tropics suppositories will require to be made up with an extra amount of wax.

Iodine.—No preparation has yet been discovered which is so potent as potassium iodide, but unfortunately there are so many people who cannot take it. A mixture of the sodium and ammonium salts is better tolerated, but an idiosyncrasy may be shown to every inorganic salt, in which case an organic salt should be tried, for preference iodoglidine. The non-staining iodex ointment is an excellent local application.

Arsenic.—Fowler's and Donovan's solutions are useful alternatives, but the powerful specific is salvarsan, and its derivative neosalvarsan. Neosalvarsan is possibly not quite so strong as salvarsan, but it is easier to use, and causes fewer toxic symptoms. Moreover, intravenous injections can be given in the consulting room, and the patient allowed to go home immediately afterwards. Both can be used for intramuscular injections, but the necessary bulk is so great, that much pain and induration may follow. Another great disadvantage of the intramuscular route, which necessitates several injections, is that, as there is no guide as to the amount of the drug that has been absorbed, there is no indication when it is safe to repeat the injection. "Ioha" is the best preparation of salvarsan for intramuscular use, and for neosalvarsan the proportion of 1 gm. dissolved in 22 c.c. of pure distilled water.

Intravenous Injections.—Before submitting a patient to this treatment he should be thoroughly examined and prepared as for an anæsthetic, in the matter of aperients and diet.

Salvarsan—

Dose for man, 0·4–0·6 gm.
Dose for woman, 0·3–0·45 gm.
Dose for child, 0·001 gm. per pound weight.

The glass tube containing the powder should be thoroughly examined before the contents are dissolved, to see that there has been no air inlet.

The contents of one tube of salvarsan should be slowly dissolved in three or four ounces of warm physiological 0·9 per cent. saline which has been prepared with freshly distilled water, in a ten-ounce graduated glass measure.

When the powder has completely dissolved after sufficient stirring with a glass rod, 10 c.c. of double decinormal [1] sodium hydrate solution should be added, with the result that a precipitate forms; this precipitate is dissolved by a further addition of sodium hydrate, usually about 10 c.c.—this may be either more or less, according to the actual acidity of the powder. The 10 c.c. should be added slowly, and the mixture stirred thoroughly. By using a weak solution of sodium hydrate we avoid the risk of making the solution too alkaline, and the exact quantity required is more easily estimated. When the solution is quite cleared by adding the sodium hydrate, the measure should be filled with saline up to ten ounces, and once or twice filtered through muslin or several layers of plain gauze, so as absolutely to exclude even the smallest solid particle from getting into the vein, where it might cause either a pulmonary embolism or hemiplegia. Ten ounces must be considered the maximum dose.

Two points must be observed concerning the saline. In the first place, the sodium chloride must be chemically pure (Merck); secondly, the solution must not be less than 0·8 per cent. or more than 1·0 per cent. A hypotonic solution is more dangerous than a hypertonic, because the former causes hæmolysis—setting free the hæmoglobin from the red-blood corpuscles. Should this happen the patient may collapse after the injection, and there may be hæmoglobinuria. Needless to say, every vessel used should be sterile and the sodium hydrate solution should be boiled before use.

To warm the solution, a hot jacket should be placed around the measure and the whole placed in a water-bath; the jacket of gauze prevents the glass vessel from cracking. When injected the fluid should be at exactly body temperature, as the reaction following is considerably greater when it is too hot.

Another vessel filled with saline is placed by the side of the one containing the "606". The patient comes to the side of the bed and hangs his arm over, then a tourniquet [2] is placed on the arm, and the limb made to rest on a table in as comfortable a position as possible. The bend of the elbow is then sterilised by first rubbing with acetone and then with ordinary tincture of iodine.

When a vein cannot be seen it can often be felt, and should be marked out with a blue pencil to indicate its course. If this cannot be done, a vein should be exposed by an incision, either under a local or a general anæsthetic. There is no danger in a general anæsthetic, for the subsequent reaction is not in any way influenced. Hitting the bend of the elbow, or warming the arm with hot towels, will often make a vein prominent. An intravenous injection may be the simplest or one of the most difficult operations possible. A common trouble is due to the vein slipping

[1] Double decinormal NaOH or $^{n}/_{5}$ NaOH = 0·8 per cent., or 8 gm. to the litre of distilled water; normal sodium hydrate being a 4 per cent. solution.

[2] The simplest and best tourniquet is some rubber tubing, which should be wound tightly around the arm and the two ends fixed with pressure forceps, which can be removed without disturbing the limb.

about when the needle tries to pierce it; extending the arm as much as possible, or pulling the skin taut to fix the vein, may prevent this.

The solution can either be injected or infused, injection being far preferable, as—

1. The needle is not so easily dislodged. If this should occur while the solution is flowing in, by infusion some must escape into the tissues before the flow can be stopped; with the syringe merely a few drops need escape, as the tap can be turned off at once.

2. The operator has more control over the proceedings.

3. There is less danger of air or a solid particle gaining access to the vein. Air is easily seen in the syringe and remains at the top, never coming over the centre of the outlet unless the piston is pushed right home. A solid particle is also seen; it falls to the bottom of the syringe and is not disturbed, provided that the solution is injected slowly and steadily and the piston not rammed home.

4. The operation is pleasanter from the patient's point of view, because it is so much quicker.

5. The risks which are alleged to follow injection, and not infusion, do not exist in actual practice.

6. The operation can be performed without an assistant, and there is practically no apparatus to carry about.

A good syringe is one invented by Schreiber, and made by the firm B. B. Cassell, Frankfurt a. M. The cannula is bayonet-shaped, bent, and fixed to a three-way metal stop-cock, so that the fluid can be sucked up from the vessel and injected directly into the vein. The needle has also a plate at its base upon which a finger can rest to keep it steady. The one disadvantage of this syringe is that the whole apparatus is rigid; therefore the slightest movement of the syringe may be sufficient to dislodge the needle.

To overcome this difficulty, Allen & Hanburys have constructed for me a needle, which is 1¼ in. in length, behind which is a slightly concave metal plate which rests on the arm and is fixed by a piece of tape which runs under a metal bridge and is tied under the arm. This needle is fixed by means of a bayonet-catch to the three-way stop-cock; but the connection between the needle and the bayonet-catch is made by a piece of thick rubber tubing, so that every movement of the stop-cock or syringe behind is broken by this flexible connection and does not affect the needle.

The all-glass syringe, which should hold 20 c.c., fits on to the stop-cock by means of a piece of stout rubber tubing, instead of being inserted into a metal tube, which may not fit every syringe.

The syringe is first filled with saline solution and all air expressed both through the tubing and the needle, then the needle is inserted into the vein, and fixed with the stop-cock open. If the vein has been pierced, which can at once be told by the touch, or by blood flowing back into the syringe, the tourniquet should be removed and some saline injected. If the cannula is not completely in the vein, the saline will produce infiltration; this being the case, the needle should be withdrawn and another vein chosen, as it is most important to prevent any of the '606' solution getting under the skin, as considerable pain is caused thereby. If much escapes there will be painful induration and œdema of the arm, which takes weeks to disappear. When the solution has all been injected, some saline should finally be used to avoid leakage of a drop or two of "606", which is done by transferring the tubing from the "606" vessel to the one containing saline. If, during the injection, the needle slips and some of the solution escapes—the patient complaining at the same moment of a burning sensation—one should immediately take the needle out, apply a tourniquet to the arm, and allow the vein to bleed, which will often prevent infiltration forming. If the injection is skilfully done, the patient has no pain. In no circumstances must the preparation be injected in a concentrated form, and great care should be taken not to inject it too quickly.

Neosalvarsan.—1·5 gm. neosalvarsan equals 1·0 gm. salvarsan. Neosalvarsan oxidises quickly, and the oxidised product is toxic, therefore the solution must be prepared immediately before use and not shaken or stirred more than is absolutely necessary. The water in which the powder is to be dissolved must be warm enough to inject, and not above 30° C., and should be warmed before the powder is dissolved. Apyrogenetic water must be employed, without the addition of NaCl or NaOH 35 c.c. to 0·1 gm. of powder. The average dose can vary between 0·45 and 0·9 gm. Both salvarsan and neosalvarsan can be injected intravenously at weekly intervals.

The best procedure of treating syphilis in its various stages is, in the primary and secondary stages to give as many weekly injections of salvarsan or neosalvarsan as are necessary to procure a negative Wassermann's reaction in the blood withdrawn the day of the last injection. By this means the patient gets one injection after his blood becomes negative. In the primary stage between three and five injections will be required and in the secondary between five and nine. In the primary stage an examination of the blood should be made before treatment is begun. In both cases four courses of eight weekly intramuscular

injections of mercury should also be given and iodides prescribed for three weeks after each course, then six months, and a year later the Wassermann's reaction should be tested and a provocative injection of salvarsan given before a cure can be pronounced.

In the latent stage, diagnosed by giving a provocative injection of salvarsan, the treatment should be the same as above described. It is no use giving a provocative injection unless at least six months have elapsed since the patient last had an injection.

In the tertiary stage, when a cure in the strict sense of the word is practically unattainable, it is best to prescribe two injections of salvarsan to get rid of the symptoms, with a subsequent course or two of mercury and iodides.

In syphilis of the nervous system salvarsan should only be urged in cases of cerebro-spinal meningitis. In tabes it may occasionally do good when mercury has failed, but an aggravation of symptoms may occur. In General Paralysis of the Insane salvarsan should never be prescribed.

In congenital syphilis salvarsan should only be given when mercury fails to cure the symptoms, and mercurial treatment should be continued for at least three years. The treatment should be intermittent and alternating, *i. e.* one course should consist of inunctions, another of Hydr. c̄ Cret. given internally, and another of wearing clothing next to the skin which has been impregnated with mercury.

Pregnant syphilitic women should be given four or five injections of salvarsan as soon as conception is known to have occurred, and mercury continued throughout pregnancy.

Last but not least, oral hygiene should never be omitted when a patient is taking mercury; cleaning the teeth with pebeco and washing out the mouth and gargling with potassium chlorate or a 1 in 20 solution of perhydrol after each and every meal should be considered imperative. A lotion containing some formalin, tincture of myrrh and rhatany for hardening the gums is often useful. J. E. R. McD.

DISEASE OF UNKNOWN ETIOLOGY

RAT-BITE DISEASE

This peculiar disease, which is very common in Japan, has recently been reported in England, America and Italy. In many of its features it resembles spirochætal or protozoal diseases and is probably due to some similar germ. Ogata in Japan, indeed, believes he has discovered a sporozoon parasite, but his researches have not been confirmed. At varying periods after the bite of rats, during which time the original wound has healed and probably been forgotten, the site of the bite inflames and breaks down and constitutional symptoms develop. These briefly consist of febrile attacks, often separated by definite apyrexial intervals, peculiar erythematous skin eruptions, enlargement of glands, œdemas, pains in the muscles and joints and sometimes albuminuria. Recurrences are common, and the disease runs a prolonged course, in some instances for a year or more. Up to the present time treatment has mostly been symptomatic, though various drugs have been tried. Amongst these are quinine, antipyrin, phenacetin, aspirin, sodium salicylate, sodium sulphocarbolate, pilocarpine, arsenic and atoxyl.

Hata recently (*Münchener med. Wochenschrift*, No. 16, 1912) describes eight cases of the disease in Japan which were treated by salvarsan. In most of these marked improvement followed the injection of the drug, the temperature falling, the inflammation subsiding, the skin eruptions disappearing and the lymph glands resolving. In two cases relapses appeared, but in those the dose had been a small one, 0·3 and 0·4 gm. If further observations confirm the value of salvarsan in this disease then the probability of a spirochæte being the cause will be greatly strengthened. G. C. L.

DISEASES DUE TO TREMATODES

Distomiasis

Fasciola hepatica—Fasciolopsis buski—Paragonimus westermani—Clonorchis sinensis

Fasciola hepatica.—This, the common liver fluke, is met with occasionally in man—the diagnosis is made by finding the characteristic ova in the stools. The parasites live in the liver, inhabiting the bile ducts, and cannot, as far as we know, be influenced by drugs. Treatment must, therefore, be palliative.

Fasciolopsis buski (Synonym, *Distomum crassum*).—This is the largest trematode infecting man; it occurs in China and the East. It inhabits the upper part of the small intestine and in some instances has given rise to recurring attacks of diarrhœa with typhoid-like symptoms. Thymol or eucalyptus given as in ankylostomiasis often bring about their expulsion.

Paragonimus westermani (Synonym, *Distoma pulmonale*).—Found in Formosa, the Philippines, and in parts of Japan and China. The parasite inhabits the lungs and other tissues of man. Its presence in the lungs gives rise to a disease known by the name of endemic hæmoptysis. This is differentiated from tuberculosis by the finding of the characteristic ova in the sputum. As regards treatment, no means of expelling the parasite from the lungs have been discovered. Drugs are useless. If much fœtor and expecto-

ration exist antiseptic inhalations will be found of use. The life-history of the parasite is unknown, so prophylaxis must only be tentative. A pure water supply should be ensured and all forms of uncooked food should be avoided.

Clonorchis sinensis (Synonym, *Distoma sinense*).—Another Eastern fluke or trematode parasite inhabiting the bile ducts and gall bladder. In severe infections the liver tissue degenerates and clinically attacks of jaundice and diarrhœa are met with. There is no specific treatment, though salol has been said to be beneficial and might be tried. Removal from the endemic area to prevent re-infection is indicated. As regards prophylaxis, drinking impure water and eating raw uncooked foods should be avoided. G. C. L.

Bilharziasis. See *Schistosomiasis*.

Katayama Disease. See *Schistosomiasis*.

SCHISTOSOMIASIS

Schistosoma hæmatobium—S. japonicum.

The two diseases which require mention are (1) Bilharziasis, due to the deposit in the tissues of countless eggs laid by the Schistosoma hæmatobium worm, mostly in the bladder, urethra, ureter and rectum; this complaint is well known in Lower Egypt, the Transvaal and other parts of Africa, and (2) Katayama disease, occurring in Japan and China and affecting the abdominal organs of the alimentary canal by a deposit of the eggs of Schistosoma japonicum. The treatment of (2) is only symptomatic at present and may be included in that of Bilharziasis.

No method has yet been discovered of killing the worms in the human body. Liquid extract of male fern 15 min. three times a day, in appropriate mucilage, is the only drug of known value, not as a cure, but to mitigate symptoms. In many cases it controls or abolishes hæmaturia, allays bladder irritation and reduces temporarily the number of eggs passed in the urine or fæces. It should not be continued for more than a fortnight at a time, lest it produce poisonous effects, such as giddiness, pain in the head and epigastrium, singing in the ears and vomiting. There is no reason why a course of this drug should not be given several times in a year, alternated with courses of salol, 12 gr. three times a day, or urotropin or urodonal as urinary disinfectants. Methylene blue 3 gr. in a wafer once a week acts as a bladder analgesic, but cannot be considered a serious treatment; if given, the patient should be warned of the discoloration of the urine.

Care must be taken not to discourage the patient by letting him suppose the malady to be incurable, for it is not a pleasant thought to a refined person to be told he is infected with worms which cannot be evacuated. I have seen some neurotic patients much depressed mentally by an unnecessarily gloomy prognosis. One-fourth of the British soldiers who contracted Bilharziasis during the war in South Africa are still, after ten years, passing ova in their excreta, but there is no reason why they should not lead an ordinary life with moderate exercise.

Hæmostatic injections into the bladder for hæmaturia are dangerous, but early cystitis is relieved by washing out the bladder with boracic acid or boro-glyceride.

When the case is complicated by a vesical calculus, the lithotrite should be used, even if there is severe cystitis. Lithotomy does not give perfect results, but in boys under four years of age, when the stone is large, perineal or suprapubic lithotomy is permissible. When the patient is in the last stage of the disease, with the bladder filled with growth, in constant pain with a continual dribbling of foul urine, the only way of attempting assistance is to drain the bladder through the perineum by Cock's puncture or by suprapubic puncture, and keep a double tube in for eight to ten days. For acute retention of urine, when the bladder is full of blood clots and the catheter draws off no urine, perineal section is again called for; then gently break up the clot with the finger, wash out the bladder and the bleeding will cease; if it does not cease, wash out the bladder again with creolin solution, hot or iced. Urethral fistulæ are cured by a free excision of the fistula and the surrounding tissues.

Perineal fistulæ must be scraped with a sharp spoon and the wound left open to allow granulation; plug the wound and tie any vessels, but it is not necessary to tie in a catheter; perhaps several operations will be required for this common complication, but perseverance will effect a cure.

Bilharzial growths of the vulva must be excised. When the rectum is affected, relief may be afforded by suppositories of belladonna or by small enemata of starch and opium, or by sulphate of copper (1 in 1000). Rectal tenesmus is caused by growths near the sphincters, so help can be given by cutting away the mucous membrane and stretching the sphincters, then swabbing the rectum with a solution of chloride of zinc (1 in 10) and washing out with saline solution. Prolapse of the rectum can be treated by the lineal cautery, and if that fails to relieve, excision may be attempted, of course preserving the sphincters.

Prevention.—The eggs in excreta should be rendered harmless by patients passing them not into water but into dry latrines, where the embryos cannot develop into miracidia. Hatching can also be prevented by formalin (1 in

160). Bathing and paddling in doubtful streams or ponds must be avoided. The relative severity of Bilharziasis in Egypt as compared with other parts of Africa is probably due to repeated re-infection. F. M. S.

DISEASES DUE TO CESTODES

Tæniasis

Dibothriocephalus latus—Tænia solium—Tænia saginata

Dibothriocephalus latus, the broad tapeworm, is seldom met with in England. Its presence in the intestine is usually associated with a severe anæmia which may closely resemble pernicious anæmia. Treatment should be directed firstly to the expulsion of the parasite, secondly to dealing with the anæmia by arsenic, iron and nourishing food.

Tænia solium. Tænia saginata.—Many drugs have been advocated for the expulsion of these common tapeworms. Filix mas (male fern) still holds the first place. As the success or non-success of the treatment largely depends on how the drug is administered, the steps are given in detail.

Place the patient on liquid diet for two days. On the afternoon of the second day calomel or some other aperient is given and some soup or milk in the evening. Next morning, say at 7.50 a.m., a cup of black coffee is taken and then between 8 and 8.30 a.m. 2 or 3 capsules, each containing 30 minims of freshly prepared Extractum Filicis Liquidum are administered (*i. e.* when 2 capsules—60 min.—are given, one at 8, the other at 8.30. When 3 capsules—90 min.—are given, one at 8, one at 8.15, one at 8.30). To prevent vomiting one drachm of brandy, to which 15 min. of chloroform have been added, is sometimes given with the first dose. Two hours later a saline aperient (Epsom salts, Carlsbad salts, or sodium sulphate) is swallowed, and then after that the whole or portions of the tapeworm or worms are passed.

Precautions.—Never give castor oil as the purgative, because the poisonous filicic acid is soluble in oily substances and is then readily absorbed. Never give more than 120 min. (4 capsules of 30 min. each), this being the maximum dose that can be given with safety. The maximum dose given here is 90 min., but on the Continent the larger dose of 120 min. is often used. The poisonous symptoms that may appear are: (1) in mild cases, jaundice; (2) in moderately severe cases, violent vomiting, abdominal pain, a feeling of feebleness, syncope and somnolence; (3) in very severe cases, cerebro-spinal paralysis and death in a few hours.

Failures to expel the parasites may be due (1) to a bad quality of the drug, (2) to too copious secretions of mucus in the intestines, (3) to special powers of resistance sometimes possessed by the parasites.

The only way to be certain that one has succeeded is to find the head of the parasite, and it is important, therefore, to examine carefully all that comes away through a strainer. The head is small, about the size of a pin's head, and may easily be missed. After treatment the stools should be watched carefully. If segments appear again in about three months' time then either the head has not come away, or there have been more than one tapeworm present in the intestine. Whenever these are seen a second course of filix mas should be at once given.

Other drugs that have been employed in the treatment of tapeworm are pomegranate, sulphate of pelletierine, kousso, pumpkin seeds, turpentine, thymol and eucalyptus oil. The two latter are the usual drugs given in the treatment of ankylostomiasis, but as they frequently cause the expulsion of distomes and tapeworms when used in that disease they might be given a trial in tæniasis, especially if filix mas should prove unsuccessful.

Prophylaxis of Tæniasis.—This is largely met by the proper inspection of meat in slaughter houses, measly pork (pig's flesh infected by the *Cysticercus cellulosæ*) and beef infected with the *Cysticercus bovis* being condemned.

Prolonged cooking will destroy the cysticercus stage of the tapeworm, so all meat, especially if any suspicion attaches to it, should be well roasted or boiled. The ingestion of underdone meat is dangerous if cysts of tapeworms are present in it.

Tænia echinococcus.—Cysticercosis (Somatic tæniasis). Echinococcus disease is now usually divided up into two forms, (*a*) the form due to the *Echinococcus granulosus* (Syn. *Tænia Echinococcus*), and (*b*) the form due to the *Echinococcus multilocularis*, the latter causing the multilocular or alveolar form of hydatid disease.

The *Tænia echinococcus*, a very small tapeworm, inhabits the intestines of dogs, wolves and jackals; its eggs when taken up by man or other animals form the cysticercus stage—the well-known hydatid cysts. These cysts may occur in any of the organs of the body, and if of large size may often require surgical treatment. When in the abdominal cavity one must always remember the danger of allowing the escape of any of the fluid contents of the cyst. If such occur, a general dissemination of daughter cysts, brood capsules, or scolices leading to a multiple infection may result. Suppurating cysts such as are often met with in the liver must, of course, be dealt with surgically.

Prophylactic Treatment.—Dogs harbouring the adult *tænia* are dangerous. The intimate contact that exists between man and pet dogs at the present day, in the light of our recent knowledge, is decidedly risky. Undoubted instances of infection in this way have been recorded. Dogs, then, should be kept in their proper places and should not be handled more than necessary. Stray dogs should be destroyed and kennels should be periodically disinfected by boiling water or chemical disinfectants.

Echinococcus multilocularis.—This form of hydatid disease, though occurring in man, is chiefly found in cattle, especially in Germany, Switzerland, the Austrian Alps, Russia and Eastern Siberia. It is absent from Iceland and Australia, where the other form is so common. Dogs, as far as is known, do not participate in its spread. Until the life-history of the parasite is worked out prophylaxis must remain unsatisfactory.

Cysticercus Cellulosæ.—This, the cystic stage of the *Tænia solium,* is sometimes met with in man. It seems fairly common in India, where several cases have recently been reported. Once acquired no treatment is of much avail. Prophylactically, we must aim at the reduction of the adult worms generally, so preventing chances of infection with their ova. G. C. L.

DISEASES DUE TO NEMATODES

Filariasis

Filaria bancrofti—Filaria loa—Filaria volvulus—Filaria medinensis

Filaria bancrofti.—The adult forms of this parasite inhabit the lymphatic glands or lymphatic vessels in any part of the body, the embryos, sometimes called microfilariæ, the blood stream. No drugs, as far as is known, have any effect on either of these forms. Pathological phenomena, depending on the situation taken up by the adult parasites are not infrequent. The most common of these are filarial abscess, filarial lymphangitis, chyluria and elephantiasis. Filarial abscesses must be opened and drained; they quickly heal up after the removal of the pus. Filarial lymphangitis is often associated with high fever, rigors, vomiting and delirium. The affected part, most commonly one of the lower limbs, swells up, becomes red and painful, while the glands in the femoral region swell and are very tender. The patient should be put to bed, placed on a milk diet, the affected limb elevated and fomented with some mild antiseptic and a brisk purge given. In three or four days the temperature falls and all the symptoms subside. After repeated attacks, a certain degree of permanent swelling may remain. In chyluria and lymphuria the patient must rest in bed and avoid fatty foods. Retention of urine owing to clots in the bladder may be troublesome. Women who have suffered should not be allowed to become pregnant, as this greatly aggravates the condition.

Elephantiasis must be dealt with surgically. Short of amputation many operations have been devised to facilitate the escape of the stagnating lymph.

Filaria loa.—The adult worms live in the connective tissues, and may, in their wanderings, come into the eye. When seen here they may be seized with forceps and removed. Calabar swellings, fugitive swellings about the size of a pigeon's egg or larger need no special treatment, they go away by themselves in three to four days. There is no drug treatment.

Filaria volvulus.—This variety of filaria forms small subcutaneous tumours under the skin. They are of a permanent nature and may erode the skin and so form open ulcers. They should be excised.

Filaria medinensis.—The female guinea worm when it wishes to deposit its embryos comes to the surface and presses on the skin with its head. A blister forms over this which bursts and the embryos are discharged through the uterine opening which lies beside the mouth. There are two ways of treating the guinea worm. (1) By pouring water on the skin of the limb near the aperture daily and so getting the worm gradually to empty her uterus. After this is accomplished the end of the body is tied to a match and little by little is gradually wound out. The patient should rest in bed during this procedure and the limb should be wrapped up in some mild antiseptic. If suppuration occurs along the track of the worm it may be troublesome and will require incisions. (2) By injecting perchloride of mercury into the worm—this kills the parasite and also sterilises it. It then resembles a piece of catgut and is absorbed. Theoretically this is the better of the two ways, but practically the results are often uncertain, so much so that the first or older method is still generally adopted.

Trichinelliasis (Synonyms *Trichiniasis, trichinosis*).—The *Trichinella spiralis* (old name *Trichina spiralis*) is a common parasite of rats. The adult forms live in the intestinal canal and here give birth to embryos which are supposed to be deposited by the female into the lymphatic vessels. From here they are carried to the muscles, where they come to rest and become encysted. Pigs become infected by eating rats and ultimately show the encysted embryos in their muscles (trichinosed pork). Man eats this and so in turn acquires the infection. The dangerous time is when the embryos are passing from the intestines to the muscles.

Once in the muscles treatment does not affect them, but every effort should be made to dislodge the adults from the bowel. Calomel, salophen, salol and thymol have been recommended. The first of these is given in 10 gr. doses cautiously increasing to 20 gr. if the patient will stand it; the second in 30 gr. doses thrice daily; the third in 10 gr. doses and the fourth as described under ankylostomiasis. During the attack the general condition of the patient must also be attended to.

Prophylaxis.—Proper meat inspection and the thorough cooking of all meat, especially pork.

Trichocephaliasis.—The *Trichuris trichiura*, *Trichocephalus dispar*, or whip worm, does not appear to cause pathological symptoms. It has, however, been known to enter the appendix, and has even been blamed for producing attacks of inflammation in that organ. Its habitat is the cæcum. Drugs have little or no effect upon it. Thymol and turpentine are sometimes given and do in some instances cause its expulsion.

Prophylaxis.—All water should be boiled or filtered through a modern filter. Watercress, salads and other raw vegetables are dangerous if the areas from which they are gathered are liable to contamination with human sewage.

G. C. L.

Uncinariasis. See *Ankylostomiasis.*

Ankylostomiasis.—The treatment is practically the same whether the patient is infected with *Ankylostomum duodenale* or with *Necator americanus*, in which case the Americans call the disease Uncinariasis. Attention should be drawn to the difference between the worm-carriers who have no symptoms of disease and the worm-sick, who are in obvious need of treatment. The important aims are to expel the worms from the small intestines, to treat the anæmia and also any concurrent disease which is present.

Three vermifuges are in use—

1. Eucalyptus oil 30 min., Chloroform 45 min., Castor oil $1\frac{1}{4}$ oz., is the dose invented by Dr. Hermann of Mons, Belgium. The following routine is useful: at 6 p.m. give a saline purge, and let the patient fast all night; at 7 a.m. give half the above dose, and at 7.30 a.m. the remainder; give no food until the bowels act, when the motions must be carefully washed to see how many worms have been expelled. The treatment may be repeated in three days' time. For children and for feeble, very anæmic patients it is wiser to divide the original dose into three parts, giving one-third part every half hour. This method has been employed in Egypt, but is not popular in Porto Rico, where the physicians find it costly, disagreeable and even dangerous.

2. Thymol has been much used since its introduction by Bozzolo in 1880. It used to be given in enormous doses of 90 gr. in a morning within four hours, but I have proved that it is not necessary to give an adult any quantity larger than 15 gr. overnight and 15 gr. the next morning, provided the stomach is empty and kept so until a succeeding saline purge has acted. The remedy can be repeated in a week and at least on three or more different occasions until eggs can no longer be discovered in the fæces. Children take half doses very well. Large doses of thymol produce poisonous symptoms not unlike those caused by carbolic acid. Dangerous collapse and even death used to occur after its indiscriminate use with old people, but are seldom met with now that we have learnt not to give alcohol with it. Besides alcohol, ether, chloroform, glycerine, turpentine and oils should not be given at the same time, and contra-indications to thymol are great weakness, very low temperature, age above 60, fatty heart or kidney disease. Thymol is still the favourite drug in some tropical countries and is decidedly better than β-naphthol for out-patients because the latter requires more care in previous starvation.

3. β-naphthol is extensively used in Porto Rico and Natal. It should be as fresh as possible and must be kept in a cool place. The routine method is to give overnight Mag. Sulph. $\frac{1}{2}$ oz. and no food; next morning give

β-naphthol 30 gr.
Mucilag. Tragacanth ʒ i
Ag. Menth. Pip. ʒv at 6 a.m.;

repeat this dose at 8 a.m. and again at 10 a.m., and at 12 noon give Mag. Sulph. 6 dr. Women should be given only 25 gr. of β-naphthol, and children 5 gr. or more, according to their age. Oil of chenopodium in 15 min. doses has lately been praised in Sumatra and the Malay States.

Extract of male fern is sometimes given, but it is a very feeble expeller of this worm, even in toxic doses.

Good food, including meat, is essential between the doses of any vermifuge. The anæmia is most quickly cured by large doses of sulphate of iron, say 8 gr. three times a day, in a mixture of glycerine and water. Bone marrow is also useful, and feeble individuals will require digitalis and strychnine.

Prevention.—Cleanliness, enforced latrines or portable pails, if in mines are very important. Disinfect, burn or bury fæces. Examine miners and coolies before they are engaged. Insist on coolies wearing shoes or having their feet and legs tarred before working in soiled, damp earth. Keep hands from contact with mouth while at work. If mines must be sprinkled with water to allay dust, add salt (2 per cent.) to the water.

Ankylostomiasis ceased to be an industrial inconvenience in the Cornwall mines after the provision and control of sanitary pails, which could easily be brought to the surface, emptied and cleaned. The eggs can be destroyed by (1) burying in the ground eighteen inches deep, provided there is no running water there; (2) exposure to dry, sun-heat for one day; (3) mixing fæces with an equal quantity of Sol. Hyd. Perchlor. 1 in 200; or (4) exposure to artificial heat 113° F. or to freezing point. F. M. S.

Ascariasis.—Santonin is the anthelmintic for the *Ascaris lumbricoides.* Its toxic effect on these parasites is very marked, and after a few doses they soon come away. The drug is usually administered together with a purgative. Castor oil seems to help its action, and therefore may be employed. An emulsion of the two may be made or the santonin may be given at night, and the castor oil the following morning. The adult dose is 5 gr., that for a child of two to four, 2 gr.; six to ten, 3 gr.; twelve to eighteen, 4 gr. The dose is generally repeated three times, either on successive nights or on alternate days. Sometimes coloured vision is complained of after taking it. This soon passes off. Excessive doses may produce serious symptoms; therefore they should be avoided.

Prophylaxis.—As for the *Trichuris trichiura.* G. C. L.

Oxyuriasis.—*Oxyuris vermicularis*, the threadworm. The parasite is common in children. Its presence about the anus causes irritation and itching which causes the child to scratch the part. After this the fingers are probably sucked and so the eggs are carried back to the mouth, thus causing a re-infection. This must be borne in mind during the treatment, which is applied by means of anthelmintic enemata. Efficient drugs for these are as follows: Salt and water 1 oz. to the pint), quassia infusion, vinegar, alcohol and water or lime water. These, of course, only kill the local worms about the rectum and do not effect the high-up ones in the cæcum and colon. Granted that re-infection and auto-inoculation is prevented, however, the infection may be expected to die out in about a month on such a line of treatment.

Prophylaxis.—A pure water supply, and as for the *Trichuris.* During infection the prevention of auto-inoculation. G. C. L.

DISEASES DUE TO ARTHROPODS

Acarina (ticks).—Apart from inoculating infectious germs (spirochætes, etc.) into one, the bite of the tick *per se* may cause inflammation and septic trouble. Once the parasites are attached they should not be roughly pulled off, as if so the head will be left behind. Soaking them in oil or paraffin will generally make them loose their hold of their own accord.

Siphunculata (lice).—These parasites have recently been shown to be the vectors of the germ of typhus fever and also of the *Spirochaudinnia recurrentis*, the cause of relapsing fever.

Treatment.—Burn all infected clothing or have clothes, bedding, etc., disinfected by steam heat. Stavesacre ointment and kerosene are both good for the *P. capitis ;* hydrargyrum ammoniatum ointment for *P. pubis.* Carbolic lotion may be used for relieving the itching and disinfecting the skin.

Hemiptera (bugs).—*Prevention.*—Use iron bedsteads. Sulphur fumigations to be used where houses are infected.

Diptera (mosquitoes or flies).—Poisoned wounds may follow the punctures of these insects. By washing the parts bitten with carbolic lotion 1 in 20 these results may largely be avoided. When travelling, especially in the tropics, a good plan is to go provided with a small phial of pure carbolic acid. By sharpening the end of a match and dipping it in this a small quantity of the acid can easily be applied to the puncture of ticks and other insects.

Siphonaptera (fleas).—*Prevention.*—Cleanliness. Dogs, if admitted to houses, to be washed in Jeyes' fluid or other disinfectants frequently. Pyrethrum powders also useful. Destroy breeding-grounds where possible by soaking in boiling water frequently. G. C. L.

TREATMENT OF THE INTOXICATIONS

METALLIC POISONING, CARBONIC ACID GAS, ETC.

Metallic Poisoning

A. Acute Poisoning.

Requisites.—The following are commonly required in the treatment of the acute cases of poisoning, which are discussed in this article—

1. Stomach tube.—A soft rubber œsophageal tube 24 to 36 inches in length, connected by a piece of glass tube to a rubber tubing 18 inches long, which is attached to a glass funnel. Two sizes should be kept. No pump should be used.
2. Higginson's enema syringe.
3. Emetics.—Tin of mustard; zinc sulphate, in powders containing 30 gr.

4. Hypodermic syringe.
5. Hypodermic injections.—Morphine sulphate; pure ether; strychnine sulphate.
6. Stimulants.—Brandy; ether; tin of coffee.
7. Antidotes.—Ammonia; calcined magnesia, 4 oz.; glycerine of tannic acid, 2 oz.; magnesium sulphate, 4 oz.; potassium permanganate, 2 dr.; tincture of perchloride of iron, 4 oz.
8. Litmus paper.
9. Vinegar; common salt; washing soda.

General Principles of Treatment.—There are few general principles on which the treatment of any case of poisoning by the mouth is based.

These principles have the following objects—

1. To remove the contents of the stomach.
2. To render inert the poison remaining in the stomach and the system.
3. To support the general strength of the individual.

1. The contents of the stomach may be removed either by active washing of the organ after passage of a stomach tube, or by an emetic.

(1) *The Stomach Tube.*—The passage of this is contra-indicated where the poison is a strong acid or alkali taken in concentrated form, owing to the risk of perforating the injured wall of the stomach.

It is important that the tube be passed with as little disturbance to the patient as possible. The following method should be adopted. If possible the patient should not be lying on the floor but on a bed or table. The head is placed in its natural position, if anything a little bent forward, but certainly not bent back. The mouth is opened only sufficiently wide to allow the insertion of the forefinger and the tube. A gag, such as a cork, should be employed if there is any risk of the jaws being forcibly closed by the patient. The tube is warmed in hot water and may be lightly covered with sweet oil for 18 inches. Oil is preferable to glycerine. The forefinger of one hand is placed in the mouth and the tube guided along it to the back of the pharynx. The forefinger is then withdrawn and the tube pushed gently down. It should be passed 16 to 18 inches or until the resistance of the stomach wall is felt. No force is necessary at any point but a gentle push has usually to be given as the tube passes over the cricoid.

When the tube is in the stomach no attempt to withdraw the contents must be made until water or fluid has been poured in. Omission to take this precaution may result in serious injury to the wall. Half a pint at least should be allowed to flow in and the funnel is then held down below the level of the patient before the fluid has entirely run out of it. In this way syphon action is ensured. If no fluid is returned, the tube may be gently "milked" by the fingers so as to cause slight suction. If this fails more water can safely be allowed to run in, and the funnel then depressed again. No difficulty is usually experienced in emptying the stomach in such a manner. The washing should be repeated several times. After the first washing at least a pint of fluid should be allowed to flow in on each occasion.

(2) *Emetics.*—Certain emetics are easily prepared.

(*a*) Mustard and water.—A tablespoonful of household mustard stirred in half a pint of tepid water. This is the only emetic which has a stimulating effect. It can safely be administered by any one.

(*b*) Salt and water.—Two tablespoonfuls of common salt stirred in half a pint of tepid water.

(*c*) Zinc sulphate.—Half a drachm in half a pint of water. This should be repeated in half an hour if vomiting has not occurred.

(*d*) Apomorphine.—This should be given by hypodermic injection in doses of $\frac{1}{10}$ gr.

These emetics are not mutually exclusive, and two or more may be given consecutively. This is especially recommended in the case of the last two. Apomorphine is very depressing if vomiting does not occur, and an emetic of mustard by the mouth should also be given. Zinc sulphate is a very reliable emetic, but has some irritant action on the stomach if it fails. When once it has been given it becomes important that vomiting should occur. If this is delayed give mustard and water, and repeat the zinc sulphate in half an hour. It may be noted here that it is often extremely difficult to cause vomiting in cases of carbolic acid poisoning, and in view of the importance of emptying the stomach, the tube should be passed at once.

2. *Render Inert the Poison Remaining in the Stomach.*—The principle involved is the addition of a substance which will combine chemically with the poison in the stomach to form a harmless, or comparatively harmless, compound.

The compound formed is rarely completely non-toxic, and in most cases the stomach must be subsequently emptied as soon as possible.

The treatment in this manner of certain groups of poisons will be considered here—

(a) *Acids.*—The principle is the administration of alkalies or certain salts in order to neutralise the acids. The best substance is undoubtedly calcined magnesia. In an emergency soap and water, or the scraping from a plastered wall or ceiling may be employed. Chalk or sodium bicarbonate neutralises acid, but in doing so carbonic gas is evolved, and if the stomach has been seriously injured by a

powerful acid the distension by the gas may lead to its rupture. These methods should, however, be employed in the absence of a supply of magnesia. If nothing is available, large draughts of water help to dilute the acid.

The substances to which these methods especially apply are hydrochloric, nitric and sulphuric acid.

(b) *Alkalies.*—This includes caustic potash, caustic soda and lime. The administration of acids causes neutralisation. The best acid is dilute acetic acid which may be given as vinegar. It is inadvisable to administer diluted solutions of the stronger acids.

(c) *Protoplasmic Poisons.*—The salts of certain heavy metals, especially copper, silver, mercury and zinc, and also sugar of lead, form compounds with albumin. When the salts of these metals are taken, they act on the mucous membrane of the alimentary canal. On filling the stomach with an albuminous solution the metal will form a combination with this albumin. This is done by giving the patient the white of eggs beaten up in water. The compounds of metal and albumin are themselves toxic to some extent, and the stomach must be washed out as soon as possible afterwards. This method should be employed when these substances have been taken, except in the case of silver nitrate, for which common salt is an effective remedy.

Apart from these groups the particular method to be adopted varies for different poisons, and will be found under the respective substance in the alphabetical list below.

3. *Support the General Strength.*—There is a great tendency to collapse even when the acute symptoms appear to have subsided.

The patient should be wrapped in warm blankets with hot-water bottles. Care must be taken that no pressure is put on a tender epigastrium.

The pain and gastro-enteritis following the corrosive and severe irritant poisons lead to extreme shock. To combat this give a hypodermic injection of morphine sulphate $\frac{1}{3}$ gr., but the immediate symptoms should be allowed to subside before the injection is made.

Stimulants are usually necessary. Often it is impossible or useless to give anything by the mouth as the stomach tube may be in employment or the stomach too much injured. The stimulants used must be such as act rapidly. Thus—

(*a*) Hypodermic injections of pure ether 30–60 min.; or of brandy 1 to 2 dr.

(*b*) Enema of coffee and brandy: 3 oz. of brandy made up to 1 pint with strong coffee.

(*c*) By the mouth: sal volatile 2 dr. in 2 oz. of water, or brandy 2 oz. in water.

Diet needs little consideration, for when gastro-enteritis is marked the alimentary canal is not in a condition for digestion and absorption, and the patient has to be tided over the acute stages by stimulants. Milk should then be given and be the sole diet until the acute symptoms subside.

Water must never be withheld and the patient should be allowed to drink freely. The withdrawal of fluid from the body by vomiting and purging is often difficult to deal with. If the skin becomes inelastic, a long rectal tube should be passed and tepid (not hot) water allowed to run in slowly by syphon action from a height of 12 to 18 inches. For this the patient is turned on the left side with the buttocks slightly raised by placing a pillow below. A pint at a time should be run in if possible.

Purging should not be checked in the earlier stages, but if it continue starch and opium enemata should be given.

The patient must not be left alone. The opportunity may be seized to repeat the dose or attempt an alternative method if suicidal, and in any case the possibility of rapid collapse is present in most forms of acute poisoning.

Treatment of Cases where the Poison is not known.—It may happen that a summons comes to a case where the causal agent is not known. The following rough outline of signs and symptoms may be of assistance in diagnosis and treatment—

1. Vomiting.
   - Strong acids (acid vomit) and alkalies (alkaline vomit).
   - Arsenic.
   - Antimony.
   - Corrosive sublimate.
   - Phosphorus.
   - Silver nitrate.
2. Vomiting and rapid purging.
   - Arsenic.
   - Antimony.
   - Corrosive sublimate.
   - Phosphorus.
3. Coma.
   - Gas poisoning.
   - Opium.
   - Alcohol.
   - Veronal.
   - Overdose of any "Sedative" drug.
4. Collapse.
   - Carbolic acid (without vomiting).
   - Oxalic acid.
   - Prussic acid.
   - Following vomiting or purging from any cause.

5. Muscular spasms.
    Strychnine.
    Severe pain from acute irritant poisons may lead to powerful voluntary contraction of muscles.
6. Delirium.
    Alcohol (unpleasant).
    Atropine (pleasant).
7. Pupils contracted.
    Opium.
8. Pupils widely dilated.
    Alcohol.
    Opium (when moribund).
9. Mouth discoloured.
    Carbolic acid.
    Oxalic acid.
    Strong acids and alkalies.
10. Abdominal pain.
    May be due to any of the agents which lead to vomiting or purging even in the absence of these symptoms.

The treatment in these uncertain circumstances should follow the lines given under *General Principles of Treatment* so far as possible.

Firstly (and most important), the stomach tube should be passed and the stomach washed out carefully. The contents may give a hint of the cause by their reaction to litmus, smell, etc. A pint of water should be left in the stomach. Secondly, stimulants should be given, an enema of brandy and coffee being specially serviceable. Morphia must not be given to ease pain. The patient must be put to bed, and kept completely at rest until all risk of secondary collapse and recurrence of symptoms has passed.

Treatment of Acute Poisoning by Various Agents. *Note.*—Where several alternatives are given, the nearest remedy should be used. They are arranged in the order of efficiency. Hypodermic injections are given in doses for an adult. Antidotes by the mouth depend on the amount and concentration of the poison and not on the age and size of the patient.

Acids (Strong). *Symptoms.* — Instantaneous burning pain from lips to abdomen. Difficulty in speaking and swallowing. Vomiting of highly acid fluid containing altered blood or shreds of mucous membrane. No diarrhœa. Extreme collapse. Subnormal temperature. Mind remains clear. Retention or even suppression of urine.

Treatment.—Emetics unnecessary. Stomach tube not to be used in cases of nitric and sulphuric acid. For other acids the tube should be used with care.

Give calcined magnesia $\frac{1}{2}$ oz. to a tumbler of water; or wall-plaster, chalk, or washing soda stirred in water; or large draughts of soap and water. With stomach tube use these for washing. Wrap in warm blankets with hot-water bottles. Next give olive oil 4 oz. in a pint of water; white of eggs (four) and water; or milk. Inject hypodermically morphine sulphate $\frac{1}{3}$ gr. Rupture of the stomach may necessitate operation. Passage of a catheter may become necessary owing to retention of urine.

Alkalies (Strong). *Symptoms.*—Instantaneous onset. Resemble those of strong *acid* poisoning, but purging is common. The vomit is alkaline.

Treatment.—Stomach tube not to be used, if patient can swallow. Give freely vinegar, $1\frac{1}{2}$ oz. in a tumbler of water; or lemon juice or citric acid in water; or acetic acid well diluted or large draughts of water. With stomach tube use these for washing also.

Next give *olive oil*, 4 oz. in a pint of water; or white of eggs (four) and water; or milk.

Inject hypodermically morphine sulphate $\frac{1}{3}$ gr.

Ammonia. *Symptoms.*—Burning pain with marked sensation of suffocation.

Treatment.—Stomach tube usually necessary as patient cannot swallow. Vinegar. Olive oil. Morphine (*vide* Alkalies). Tracheotomy may be necessary owing to œdema of glottis.

Antimony. Fatal dose varies greatly.

Symptoms.—Onset in $\frac{1}{4}$ to $\frac{1}{2}$ hour; may be delayed longer. Gastro-enteritis, vomiting especially marked. The vomiting may empty the stomach completely, and life should never be despaired of even after enormous quantities of tartar emetic. Symptoms resemble arsenic poisoning and cholera.

Treatment.—If vomiting has not occurred, use stomach tube and emetics with large draughts of tepid water. Encourage vomiting.

Give glycerine of tannic acid, 2 dr. in a tumbler of water, or tannic acid, $\frac{1}{2}$ dr. in a tumbler of water, or large drinks of strong coffee or tea. If vomited repeat each time. (Antimony forms an insoluble compound with tannic acid.)

Wrap in warm blankets with hot-water bottles to the feet. As vomiting subsides, give white of four eggs in water or milk. Inject ether 30 min., hypodermically, or brandy and coffee enema; repeat at short intervals.

Rectal injections of saline if possible. Later, when acute symptoms have subsided, inject morphine sulphate $\frac{1}{3}$ gr. hypodermically to relieve pain.

Tendency to collapse is usually marked.

Aqua Fortis.—Synonym for nitric acid.

Arsenic.—Fatal dose, 2–3 gr.

Symptoms.—Resemble antimony poisoning.

Treatment.—Stomach tube. The stomach must be thoroughly and repeatedly washed out. Emetics in absence of stomach tube. Give freshly precipitated hydrated ferric oxide, prepared thus—

Place in a tumbler of water an ounce of tincture or solution of perchloride of iron, and add two tablespoonfuls of washing soda or *dilute* ammonia. Filter the bulky precipitate through a handkerchief and dissolve it in a tumbler of hot water. Give in large quantities, frequently repeated. If this is not available give magnesia or olive oil or castor oil frequently and in large amounts.

As vomiting subsides, give white of four eggs in water or milk. Wrap in warm blankets with hot-water bottles to feet. Give stimulants freely. Inject ether 30 min. hypodermically or brandy and coffee enema; or brandy 1 dr. hypodermically; or brandy by the mouth. Repeat frequently.

When acute symptoms have subsided, inject morphine $\frac{1}{3}$ gr. hypodermically.

Barium Salts. *Symptoms.*—Gastro-enteritis.

Treatment.—Stomach tube or emetics. Give sulphates in some form (in order to convert barium into the insoluble sulphate) and then wash out stomach, thus: Sodium sulphate (Glauber's salts), 1 oz. doses in water, or magnesium sulphate (Epsom salts) 1 oz. doses in water. Wrap in warm blankets with hot-water bottles. Give stimulants. When acute symptoms have subsided inject morphine $\frac{1}{3}$ gr. hypodermically if much pain.

Bichromate of Potash. *Symptoms.*—Gastro-enteritis. Powerful irritant. Mouth and lips stained yellow.

Treatment.—Stomach tube or emetics. Give magnesium carbonate, or chalk, $\frac{1}{2}$ oz. in half a pint of milk. With stomach tube use this for washing also. Then white of four eggs in water. Warmth. Stimulants. Inject morphine $\frac{1}{3}$ gr. hypodermically if much pain.

Carbolic Acid. *Symptoms.*—On swallowing a burning sensation is felt but the anæsthetic action prevents subsequent pain. This usually also prevents vomiting even with emetics, though occasionally it is profuse. Carbolic acid is often taken in large amounts, is rapidly absorbed and acts on nervous centres. Consequently there is rapid onset of unconsciousness with collapse. The smell of the breath is often characteristic, and there may be white or brown patches where the acid has been in contact. After consciousness is regained, *rapid collapse and death may still occur.*

Treatment.—Carbolic acid acts with extreme rapidity and no time must be lost. Stomach tube carefully, wash stomach repeatedly with magnesium sulphate (Epsom salts) or sodium sulphate (Glauber's salts), 1 oz. to a pint of warm water. Use large quantities, continue until no smell of carbolic acid, leave a pint in stomach. Or use saccharated lime water, one part to three of water. If tube not available, give above solutions to drink.

Apply warmth to body, warm blankets, hot-water bottles or friction. Artificial respiration if necessary. Give stimulants freely, brandy by rectum, and ether 30–60 min. hypodermically. Later give white of eggs in water freely, or milk, and injections of saline by rectum. Watch carefully lest collapse occurs after recovery of consciousness. If pulse is feeble, give strychnine $\frac{1}{30}$ gr. hypodermically.

Carbonic Acid Gas (CO_2). *Symptoms.*—Heaviness and throbbing in head. Progressive loss of muscular power. Insensibility. Lividity.

Treatment.—(CO_2 is heavier than air and accumulates near the floor.) Fresh air. Artificial respiration (sixteen to the minute), not to be stopped for any reason, and not to be abandoned for several hours. Inhalation of oxygen, using Leonard Hill's mask or holding jet close to mouth. Friction, warmth to extremities. Occasional inhalation of ammonia. Alternate hot and cold douches to chest. Strong coffee enema (1 pint). Inject ether, 30 min. hypodermically, or brandy.

Carbon Monoxide (CO). *Symptoms.*—Rapid weakness of mental and muscular power. Insensibility.

Treatment.—*Vide* Carbonic Acid Gas.

Caustic Potash. }
Caustic Soda. } *Vide* Alkalies.

Chlorate of Potash.—Emetics. Stomach tube.

Coal Gas. *Vide* Carbonic Acid Gas.

Copper Salts. *Symptoms.*—Metallic taste, gastro-enteritis, collapse.

Treatment.—First, large quantities of white of eggs and milk. Then stomach tube (tepid water) or emetics. Copious drinks of tepid water. When acute symptoms subside, inject morphine $\frac{1}{2}$ gr. hypodermically.

Corrosive Sublimate. *Symptoms.*—Metallic taste, gastro-enteritis, collapse.

Treatment.—First give large quantities of white of eggs in water. Then stomach tube and wash with water, or give emetics. (Mercury forms an albuminate which is toxic and must be removed at once.) Leave some white of egg in stomach. Warm blankets and hot-water bottles. Stimulants. Later inject morphine $\frac{1}{3}$ gr. hypodermically.

Cyanide of Potassium. *Symptoms.*—Onset in one to two minutes. Insensibility. Respirations slow and irregular. Pulse fails. Breath may smell of almonds.

Treatment.—Artificial respiration. Stomach tube or emetics, or large draughts of water. Stimulants. Inject ether 30 min. subcutaneously, and repeat in a few minutes. Inhalation of

ammonia on a handkerchief. Alternate douches of hot and cold water on the chest. The following may be tried as a chemical antidote, but not at the expense of preceding measures: ferrous sulphate 10 gr. in 5 oz. of water, followed by magnesium carbonate 1 dr. in a little water.

Fly Papers. *Vide* Arsenic.

Hydrocyanic Acid. *Vide* Cyanide of Potassium.

Hydrochloric Acid. *Symptoms.—Vide* Acids.

Treatment.—Give calcined magnesia $\frac{1}{2}$ oz. in a tumbler of water, or wall-plaster, chalk, washing soda, well-diluted ammonia, or well-diluted sal volatile in water, or large draughts of soap and water. Repeat if vomited. Wrap in warm blankets with hot-water bottles. Give white of eggs in water or olive oil, 4 oz. in a pint of water, or milk. When acute symptoms subside, inject morphine $\frac{1}{3}$ gr. hypodermically.

Lead Salts. *Symptoms.*—Metallic taste. Colic. Thirst.

Treatment.—Stomach tube or emetics. Give magnesium sulphate (Epsom salts) $\frac{1}{2}$ oz., or sodium sulphate (Glauber's salts) $\frac{1}{2}$ oz., or dilute sulphuric acid $\frac{1}{2}$ dr. in a tumbler of water. Next milk or white of eggs in water. Warmth to abdomen. Inject morphine $\frac{1}{3}$ gr. hypodermically if much pain.

Lunar Caustic. *Vide* Silver Nitrate.

Mercury Salts. *Vide* Corrosive Sublimate.

Muriatic Acid. *Vide* Hydrochloric Acid.

Nitric Acid. *Symptoms.—Vide* Acids.

Treatment.—Give calcined magnesia $\frac{1}{2}$ oz. in a tumbler of water, or chalk, washing soda, wall-plaster, well-diluted ammonia; well-diluted sal volatile, or soap and water in large quantities. Repeat if vomited. Wrap in warm blankets with hot-water bottles. Next give olive oil, 4 oz. in a pint of water, or white of eggs in water or milk. When acute symptoms subside, inject morphine $\frac{1}{3}$ gr. hypodermically. If larynx affected, tracheotomy. Do not pass stomach tube if patient can swallow or is vomiting, but if not, pass tube in preference to doing nothing. The possibility of perforation of the stomach wall must be remembered.

Oxalic Acid. *Symptoms.*—Onset and progress of symptoms very rapid. Acid taste. Pain in stomach. Vomiting. Rapid collapse and cardiac failure from action after absorption.

Treatment. Give saccharated lime water $\frac{1}{2}$ oz. in 2 oz. of water, or chalk or wall-plaster in water in large amounts, or lime water. If vomiting has not occurred, pass stomach tube with care, and wash with lime water. Stimulants. Ether 30 min. hypodermically, or brandy. Repeat saccharated lime water half hourly for six doses. Give milk freely.

Do not give sodium and potassium salts (*e. g.* soap, sodium carbonate, washing soda). The compounds with oxalic acid are very poisonous.

Perchloride of Mercury. *Vide* Corrosive Sublimate.

Phosphorus. *Symptoms.*—May be a garlicky taste. Latent period of $\frac{1}{4}$–2 hours or more. Then garlicky eructations. Luminous vomiting. Purging. Collapse. Death or recovery from these symptoms. A few days later secondary symptoms of acidosis: jaundice, vomiting and acetonuria.

Treatment.—Primary stage. Stomach tube or emetics. Wash stomach with potassium permanganate 1 per cent. solution, or sanitas (or water, if others not available). Leave some in stomach. Then give these to drink: potassium permanganate 1 per cent. solution diluted with three times as much water. Later give magnesium sulphate, $\frac{1}{2}$ oz. in 4 oz. of water. Also milk or white of egg in water. When these symptoms subside, give alkalies to prevent secondary stage: sodium bicarbonate 1 dr. four hourly. Also sugar and water frequently. (1 oz. of sugar four times a day.) Continue for five days at least.

Potash. *Vide* Caustic Potash.

Potassium Chlorate. *Vide* Chlorate of Potassium.

Prussic Acid. *Vide* Hydrocyanic Acid.

Rat Pastes.—"Rough on Rats," and Simpson's contain arsenic. Roth and Ringeisen's contain arsenic and phosphorus.

Salts of Lemon.
Salts of Sorrel. } Synonym for potassium binoxalate. For treatment *vide* Oxalic Acid.

Sewer Gas.—Treatment as for Carbonic Acid Gas.

Silver Nitrate. *Symptoms.*—Gastro-enteritis. Vomit may contain white flakes turning black on exposure to light.

Treatment.—Common salt, two tablespoonfuls in a tumbler of water. Repeat after vomiting. Then emetic of mustard. White of eggs in water in large quantities.

Soda. *Vide* Caustic Soda.

Spirits of Salts. *Vide* Hydrochloric Acid.

Sugar of Lead. *Vide* Lead.

Sulphuric Acid (Swallowed). *Symptoms.—Vide* Acids.

Treatment.—Large draughts of soap and water. Calcined magnesia $\frac{1}{2}$ oz. in 5 oz. of water, or wall-plaster, chalk, washing soda, sodium bicarbonate in water, or water alone if nothing else available. Give the nearest of these before looking for anything else. Repeat after vomiting. Later give olive oil, 4 oz. in a pint of water, or white of eggs in water, or milk. Wrap in warm blankets with hot-water bottles. Inject morphine $\frac{1}{2}$ gr. hypodermically. The possibility of perforation of the stomach wall must be remembered.

Sulphuric Acid (Thrown).—Wipe off the acid and bathe with soap and water, or water con-

taining soda or bicarbonate of soda. If the eyes are involved wash them gently with water and then with a lotion of sodium bicarbonate and water (5 gr. to the ounce). Then drop in a few drops of castor or olive oil. Keep quietly in bed. Give stimulants, especially brandy. Then inject morphine sulphate ⅓ gr. hypodermically.

Tartar Emetic. *Vide* Antimony.

Vermin Killers.—"Rough on Rats," and Simpson's contain arsenic. Roth and Ringeisen's contain phosphorus and arsenic. Battle's and Butler's contain strychnine.

Vitriol. *Vide* Sulphuric Acid.

Water Gas. *Vide* Carbon Monoxide.

Weed Killers. *Vide* Arsenic.

White Precipitate. *Vide* Corrosive Sublimate.

White Vitriol. *Vide* Zinc.

Zinc Salts. *Symptoms.*—Profuse vomiting. Gastro-enteritis.

Treatment.—White of eggs and milk. Sodium carbonate or washing soda in large quantities of warm water. Strong tea. Inject morphine ⅓ gr. hypodermically, when acute symptoms have passed.

For other poisons see *Pharmacological* section under respective drugs.

B. Chronic Poisoning

The common chronic forms of metallic poisoning are due to arsenic, lead, mercury and, rarely, phosphorus. "Brass-founder's ague" is due either to copper or arsenic. In all cases the treatment is removal from the cause, and general treatment for the symptoms.

Arsenic.—The disturbance of the alimentary canal must be corrected, for which Mist. Cretæ. may be employed. A light diet without alcohol should be given. The mucous membranes of the eye and mouth may be inflamed or ulcerated, in which case they should be bathed with boracic acid lotion. Tonics and a full diet should be given as soon as the intestinal irritation subsides. Arsenical paralysis needs rest in bed, with the administration of strychnine and the employment of massage and electricity. Pigmentation of the skin needs no treatment.

Lead.—Three main sets of symptoms occur in chronic lead poisoning.

1. *Attacks of Colic and Constipation.*—To ease the pain in a paroxysm hot fomentations should be applied to the abdomen, and tincture of opium, 20 min., given by the mouth. The bowels must be opened at once by an enema of olive oil or hot water. Then an ounce of castor oil by the mouth. Subsequently belladonna and sulphates should be administered.

℞ Magnesii Sulphatis, ʒ ½
Acidi Sulphuris Dil., ♏ x
Tincturæ Belladonnæ, ♏ v
Aquæ Menth. Pip., ad. ℥ i

To be taken three times a day until the colic has subsided and the bowels are well opened. The belladonna should then be omitted and the sulphates continued. The diet should be light as long as the intestinal symptoms are present.

2. *Lead Palsy.*—In the great majority of instances this involves the extensors of the wrists. When severe the hands must be supported by splints or slings. Massage and electricity should be employed and strychnine administered.

3. *Lead Encephalopathy.*—These cases may closely simulate cerebral tumours. The patient must be kept in bed and sulphates administered. In all forms of lead poisoning tonics are necessary, especially iron: thus ferrous sulphate 3 gr. may be added to the sulphate mixture. Potassium iodide, to assist the elimination of lead from the tissues, should not be given while acute symptoms persist, but may then be used in 5 gr. doses three times a day.

Mercury.—With very small doses of mercury gingivitis and salivation may occur. The administration must be stopped immediately. Mouth-washes, such as myrrh and borax, must be used frequently. If the alimentary tract is irritated, Pulvis Cretæ Aromaticæ 30 gr. three times a day is useful. Constipation must be avoided. Tonics should be given when the acute symptoms subside, and a full diet.

H. L. T.

ALCOHOLISM AND OTHER DRUG HABITS

All the habit-forming drugs referred to in this article exhibit certain effects in common—

1. In the early stages of the habit they give rise to *euphoria*, that is, a temporary sense of comfort and well-being; this constitutes the essential motive of indulgence. Euphoria is a brain effect and varies in character and degree with the drug and the dose of the drug.

2. Taken regularly they establish *tolerance*—that is, a condition in which they cease to produce euphoria and other physiological effects unless given in large and increasing doses. Such *acquired* tolerance arises most readily through the use of frequent, small, but progressively increasing doses, each of which is but just sufficient to cause moderate euphoria. The steady spirit drinker, especially the secret drinker, offers the most familiar example.

3. Acquired tolerance, if at all marked, involves in the great majority of cases *intolerance of sudden withdrawal*. That is to say, the sudden withdrawal of the drug, unless compensated or obscured in some way, is followed by mental misery and definite physical symptoms. Such *sudden abstinence phenomena* are fairly distinctive for each individual drug: in character they are

for the most part the opposite of the mental and physical symptoms which constitute the special euphoria conferred by the drug; and they vary in severity with the degree of tolerance acquired and with the suddenness of withdrawal. They may be extremely severe, and in some cases have led to insanity and, directly or indirectly, even to death.

4. Following a period of abstinence of doubtful duration, acquired tolerance is *lost*. Doses of the drug previously taken with little effect may then prove disastrous, even fatal.

5. Those who have recovered from any of the drug habits here referred to can never again hope to use the drug in question in moderation. Thenceforward they must consider themselves a class apart in this one respect, namely, that in their case moderate use will inevitably lead to excess: total, and permanent total, abstinence is for them the only course. Furthermore, what is true of the use of the same drug is only slightly less true of the use of any other of the drugs in the series.

All the above five propositions have a distinct bearing on the question of treatment.

Alcoholism

The goal of treatment, then, is the establishment of permanent total abstinence; and the first indication is the withdrawal of alcohol. Now the mode of withdrawal—whether the drug should be carefully *tapered* off or suddenly withheld—will depend on the presence or absence of acquired tolerance. Moreover, when tolerance is present, its degree will determine inversely the rapidity of tapering which is expedient.

Unlike most other drug habits, alcoholism exists in two forms: it may be intermittent—dipsomania, pseudo-dipsomania; or continuous—chronic inebriate alcholism, chronic sober alcoholism.

Intermittent Alcoholism.—In both varieties (dipsomania and pseudo-dipsomania), at least in typical cases, the drinking is short-lived and furious: tolerance has no time to become established. Hence tapering is unnecessary. Not only so, it is actually injurious, greatly increasing the difficulty of managing the case. Every dose of alcohol given, at any rate in all but the last stages of the paroxysm, markedly intensifies the craving, although it may be admitted it affords momentary relief. If, on the other hand, the patient can be kept for one, two or three days (the exact time varying with the case) without any alcohol, all craving ceases, often with remarkable suddenness. But it is impossible in most cases, without having full legal control of the patient, simply to withhold alcohol. Hence, in both private and sanatorium practice, resort must be had to drugs for assistance. Here, fortunately, we have in apomorphine a drug which accurately fits all such emergencies. Indeed, it is not too much to say that without the assistance of apomorphine it would be impossible to carry on with any satisfaction a free sanatorium into which were frequently admitted acute cases of alcoholism.

Apomorphine is always given hypodermically, and the most convenient solution, which should have been made somewhat recently, is 1 in 200. The dosage will vary with the state of the patient. If intoxicated, especially if noisy or violent, a full dose is demanded. In textbooks this is set down at $\frac{1}{10}$ gr., equal to 20 min. of the above solution. But though there is no death recorded, severe collapse is stated to have followed this dose occasionally. Accordingly, for some years 15 min. has been the maximum dose I have used. This is ample, and its effect can only be described as dramatic. Just previously the patient may have been wildly uproarious, even actively homicidal, necessitating several attendants to control him. Yet always within ten minutes, usually within four or five, he is placidly asleep. The first effect of the injection is pallor: the patient becomes suddenly quiet, his muscles relax, and he vomits. Immediately vomiting ceases he is asleep. Sometimes, indeed, he is asleep even before the diaphragmatic spasms have ceased: hence a possible danger of choking unless he is carefully watched for a time. In one case only has 15 min. failed to cause emesis: it has never failed to cause sleep, though used in upwards of 200 cases. The sleep which ensues is at first deep, but within a hour or so becomes light, and the patient is easily roused. It always lasts for a couple of hours: sometimes it endures for seven or eight.

But in any case when he awakes, the patient's mental condition is entirely altered. He may be sober: he is at least quiet and tractable; and, moreover, he is free for the time being from any craving for alcohol. The craving may return, however, and then it is necessary to repeat the injection, it may be several times at intervals of a few hours. These succeeding injections should be quite small, 3 to 6 min. being sufficient. Doses of this size are rarely emetic. There is a little facial pallor, a sensation as of the commencement of sea-sickness, perhaps slight malaise, with a sudden subsidence of the craving for alcohol, followed by a light and short doze.

In addition to quelling each marked recurrence of the dipsomaniac craving by small prompt injections of apomorphine, it is nearly always advisable to administer at bedtime a *full* dose of some more enduring hypnotic: this at any rate for the first night or two after the patient comes under treatment. Usually, perhaps, veronal is most suitable. But sulphonal,

trional, paraldehyde or chloral may be substituted. If the patient has taken hypnotics previously and knows the dose which is for him efficient, it will be expedient not to alter the drug: thus the dangers of under- and over-dosing are avoided.

Continuous Alcoholism.—Practically always in both varieties of this form there is established some degree of tolerance of alcohol. This degree, which of course varies widely, must be first determined with some approach to accuracy. Commonly—almost invariably in sober alcoholism—the patient can say exactly what he takes and when he takes it. But in not a few cases—especially, of course, in inebriate alcoholism—the amount taken cannot be stated or is deliberately concealed, that is, understated. Then it is necessary to institute a short tentative period of abstinence. Very soon, in cases of high tolerance, abstinence symptoms appear. Such are nervousness, restlessness, irritability, muscular tremor on voluntary movement, and insomnia, perhaps also anorexia and nausea. By studying these and the effect upon them of known doses of alcohol, it is easy with a little practice to estimate with sufficient accuracy the degree of tolerance acquired. This may vary from quite small amounts to 20 or 25 fl. oz. of spirits: it is rarely more. And it is only the larger amounts (from 10 fl. oz. upwards) which are of importance clinically.

Having determined the degree of tolerance (which, except in strictly sober alcoholists, does not of necessity coincide with the habitual amount of alcohol taken) tapering should be at once instituted. Quite the most important point is that *no sudden large* reduction should be made *during the first three or four days*. Supposing tolerance to be estimated at 20 fl. oz. of whisky per diem (*i. e.* in the twenty-four hours), the first reduction should be to 18 fl. oz., certainly not less than 17; the next to 16, not below 15; and the next to 13 or 12. A safe rule is to deduct 2 fl. oz. per diem. When, however, the amount has fallen to 4 or 5 fl. oz., further tapering is unnecessary: indeed, many patients themselves suggest final withdrawal at this stage. There is nearly always some albuminuria in chronic alcoholism, and the degree of albuminuria may or may not be an accurate index of the degree of tolerance established. But whether this is so or not, the presence of much albumen certainly increases the necessity for tapering as against sudden withdrawal.

It will be observed that alcohol tapering represents roughly an arithmetical progression: herein differing essentially from morphine tapering, as will be pointed out later.

The tapering process is greatly facilitated by the use of bromide of sodium, given thrice daily in dram doses. In addition it is often, if not usually, advisable to give a special hypnotic at bedtime. The hypnotics used are the same as those recommended in intermittent alcoholism. One great advantage of tapering is that it renders an ordinary full dose of any hypnotic sufficient to ensure a good night's sleep. Under sudden withdrawal, enormous, even dangerous, doses would be necessary in many cases.

Abstinence Phenomena of Chronic Alcoholism.—The minor phenomena have been mentioned: the major include *delirium tremens* and *alcoholic epilepsy*.[1] The treatment of these complications may be considered under the heads of (1) preventive; (2) abortive; and (3) in the actual attack.

The preventive treatment in both complications is that of alcoholic tolerance, and has just been described. Given sufficient time, it should be almost invariably successful as regards delirium tremens. Fits, however, may occasionally occur, since now and then they are apt to arise in quite low degrees of tolerance—degrees which have not seemed to necessitate tapering. Moreover, they are less frequently preceded by minor abstinence phenomena than are attacks of delirium.[2]

The abortive treatment of delirium tremens can be adopted successfully only in the very early stages of the attack, when the mental symptoms are but just commencing. It consists in rapidly making up the deficiency in the alcoholic intake so that the point of tolerance is reached, or nearly so, combined with a full dose of some hypnotic should sleep not quickly follow the alcohol. Subsequently, careful tapering should be practised. Delirium tremens has been aborted also by very large doses of hypnotic drugs without alcohol, and by chloroform anæsthesia. The latter method, however, has proved fatal, nor can the former be said to be free from danger.

The treatment during a fit is that of any major epileptic attack. As regards the developed attack of delirium, it usually suffices to provide adequate, skilled attendants—two at least are always required—and to instruct them not to allow the patient out of their sight for an instant and to see that some fluid nourishment is regularly given. Whether or not alcohol should be allowed is undecided: my own experience

[1] "Both alcoholic epilepsy and delirium tremens depend primarily and remotely upon the acquisition of tolerance of alcohol, and secondly and proximately upon a sudden fall in the accustomed quantity of alcohol circulating in the . . . brain and nervous system."—*On Alcoholism*, Francis Hare, 1912, p. 154.

[2] When they are so preceded it is highly probable that delirium also is impending—that the former is merely a part of the latter.—*On Alcoholism*, Francis Hare, 1912, p. 156.

is that, though it modifies the severity of the delirium, it defers convalescence. In exceptional cases—when the delirium is prolonged beyond three full days, when the temperature rises to 101° F. or more, or when there are signs of circulatory failure—it seems essential to procure sleep by means of drugs. Hyoscine seems most likely to succeed. Commencing with $\frac{1}{150}$ gr. I have given up to $\frac{1}{80}$ gr. every six hours. The usual result is an hour or two of rather disturbed sleep following each injection.

Reference may here be made to mania à potu, pathological or maniacal drunkenness, a condition which, though sometimes confused with delirium tremens, differs essentially therefrom.[1] The treatment consists merely in a single full dose of apomorphine with confinement to bed during the subsequent sleep. This is practically always completely successful.

Treatment following Complete Withdrawal of Alcohol.—Though, as pointed out, all craving for alcohol rather suddenly ceases a few days after withdrawal, yet such freedom is not necessarily continuous thenceforward. There are recurring days on which the craving is apt to return in some degree : this at any rate in the majority of patients and for a few weeks. Accordingly, the patient should always remain under supervision and treatment for *at least* six weeks in all : often a longer period is advisable. During this time all his habits should be regularised. Regular outdoor exercise short of fatigue, regular well-cooked and well-served meals not too elaborate, at least eight hours' sleep and frequent dogmatic advice short of causing boredom —all these are necessary. The advice tendered should allow him no escape from the conclusion that total, and permanent total, abstinence from even minute quantities of alcohol is for him essential.

It should be pointed out that the taking of one small alcoholic drink re-creates the craving and leads inevitably sooner or later—sooner in the vast majority of cases—to frank relapse into alcoholism : that consequently the first alcoholic drink constitutes the relapse and immediately entails a new course of treatment even if a very short one : so the patient may start afresh with an absolutely clean sheet. The regular administration of such advice should be regarded as an item in the course of treatment, not less essential than the regular exhibition of medicines by the mouth and by the hypodermic needle. It constitutes, indeed, treatment by suggestion and is, in my experience, at least equal in efficiency to treatment by hypnotic suggestion. But here there is an important proviso. Always averse from facing unwelcome facts, the patient will inevitably discount advice tendered him by one who has acquired the reputation of being an extremist in temperance matters. Should the physician be himself convinced that abstinence is the only true temperance for the whole of the human race, he will be well-advised to conceal his opinion from his alcoholic patient. On this point there is no room for doubt.

The patient should regard himself as an individual with one special weak point to which he will always have to live down. This refers, of course, to his inability to indulge moderately in alcohol. It may even be admitted that, consequent on this necessity, he will lose some enjoyment when compared with the ordinary temperate person. But it can be safely insisted that there are numerous compensations which in the aggregate more than out-balance his limitations. Men of means who, on becoming abstainers succeed in acquiring some absorbing hobby usually do well, while for business men and others whose income has to be earned, it is always expedient at the end of their course of treatment to return straightway to their work and commence at once to recover some of the leeway for which their habit has been responsible. Prolonged change of air, holidays of various kinds, trips, *above all sea-trips*, are not only unnecessary but often actively harmful. Of all places in the world a modern passenger steamer is the worst for the ex-alcoholist.

In addition to general hygiene and systematic suggestion, a special course of medication should follow, not precede, the final withdrawal of alcohol. In the sanatorium with which I am connected the drugs in use are strychnine, atropine and red cinchona bark. The former two are given both hypodermically and by the mouth : the last in the form of a tonic. The solutions for hypodermic use are strychnine nitrate 4 gr. to the ounce of distilled water, and atropine sulphate 1 gr. to the ounce. The first injection consists of 2 min. of the strychnine solution with 1 min. of the atropine solution. This is given in the one injection thrice daily immediately after breakfast, lunch and dinner. After a day or so, the dose is raised by the addition of 1 min. of each solution. Every few days similar additions are made until the patient is receiving 7 and 6 mins. respectively of each solution. Larger doses are now rarely used. The maximum dose may be continued for perhaps a week. Subsequently the dosage is reduced by the same steps as it increased, until at the end the patient is receiving 2 min. and 1 min. respectively. The tonic contains

[1] "Mania à potu depends upon intolerance of alcohol, inherent or acquired, and is a direct result of the consumption of alcohol often in quite small quantities; delirium tremens depends upon a tolerance of alcohol which is always acquired, and is a direct result of a sudden inadequacy in the regular supply of alcohol to the blood and nervous system."—*On Alcoholism*, Francis Hare, 1912, p. 129.

strychnine solution 1 min., atropine solution 1 min., concentrated liquor of cinchona (Fletcher) 24 min., concentrated compound liquor of gentian (Fletcher) 8 min., and glycerine 1 dr., in each half-ounce dose. This is given diluted three or five times daily between meals.

Only occasionally have modifications to be made in this medication. Slight muscular twitchings demand a temporary reduction or cessation of the strychnine, and this drug may have to be omitted from the evening injection in some cases of insomnia; there are also some alcoholists in whom strychnine causes extreme irritability and nervousness. The atropine may have to be omitted should there result cutaneous irritation sufficient to prevent sleep, and in rare cases cinchona causes rather severe dyspepsia.

The use of these drugs is purely empirical. I can only express my own belief that their use as above described is of some real assistance in maintaining the freedom from the craving for alcoholic euphoria.

Management of True Dipsomania.—This is the one exception to the rule that alcoholists after withdrawal should remain under supervision and treatment for at least six weeks. The term dipsomania is often applied loosely to any case of severe paroxysmal drinking. But it should be reserved for cases in which the craving for alcohol comes on *in spite of prolonged abstinence.* Such patients usually show distinct premonitory symptoms and the paroxysms occur at more or less regular intervals. These cases are quite rare, and in them there is probably less danger of relapse into drinking during the immediately post-paroxysmal period than at any other time. What is above all necessary in their case is to recognise the commencement of the premonitory stage and bring the patient immediately under supervision and treatment. When this can be done—which unfortunately is not often—a few doses of apomorphine, perhaps reinforced by a single full dose of some more enduring hypnotic at bedtime, will usually succeed in completely preventing or aborting the threatening paroxysm. There is little to be gained by keeping these patients under close observation for more than a fortnight, unless, of course, the duration of the supervision is sufficient to cover several paroxysms, as in treatment in a licensed retreat under the Inebriates' Act.

Morphinism

Possibly because tolerance is so rapidly established, morphinism exists almost solely in the continuous form. Patients are sometimes said to suffer from intermittent or paroxysmal morphinism; but these on close inquiry almost always turn out to have some recurrent painful or distressing affection, *e. g.* severe migraine, gastralgia or insomnia. Here the craving is for relief from pain, etc., not for morphine euphoria, and such cannot correctly be regarded as morphinists. It happens, therefore, that practically all morphinists coming under treatment have already acquired distinct tolerance of the drug; and the combating of the abstinence phenomena during withdrawal is a much more formidable problem than in the case of chronic alcoholists.

Formerly it was the practice simply to withdraw the drug suddenly, and this is occasionally done even now. But it is not a possible method except in an asylum or under conditions which give the physician complete control of his patient. Nor can I regard it as justifiable in any circumstances. Except in the mildest cases, it is horribly cruel and by no means free from the danger of causing insanity (usually temporary, however), or fatal collapse (often preceded by choleraic symptoms).

Sudden Withdrawal.—Recently, however, morphine has been *suddenly* withdrawn even in severe cases by what is known as the *hyoscine method*—a method mainly elaborated by Lott in America and introduced into this country by Purves Stewart.

A quiet, well-ventilated room, preferably on the ground floor, is selected, and the patient, after a hot bath, put to bed. Special attendants are instructed to watch him constantly night and day. The medicinal treatment commences at such time as he is well under the influence of his usual quantity of morphine. Hyoscine hydrobromide $\frac{1}{100}$ gr. is first given hypodermically. This is followed by $\frac{1}{200}$ gr. every succeeding hour until hyoscine intoxication or delirium is produced. Then the $\frac{1}{200}$ gr. injections are reduced in number, being continued just often enough to maintain the delirium for twenty-four, thirty-six or forty-eight hours, in accordance with the severity of the morphinism. One or two $\frac{1}{4}$ gr. injections of morphine may be called for during the first few hours before the delirium begins, and water to drink is freely allowed. At the end of this stage, the hyoscine is stopped, whereupon the patient soon becomes rational. Then commences the second stage. Pilocarpine nitrate $\frac{1}{8}$ gr. is injected every hour or two hours until sweating begins, being continued subsequently just sufficiently often to maintain the skin moist. This ceases with the cessation of the hyoscine symptoms. The object of the pilocarpine medication is stated to be the elimination of the hyoscine. Whether this be its effect or not, it certainly relieves the patient of his parched tongue and dry skin, thus conducing materially to his comfort. During the pilocarpine stage, pains in the knees, elbows and back, sometimes cramps, arise. For these massage is recommended. For diarrhœa, 60-gr.

doses of bismuth salicylate with 6 min. of liquid extract of colo bark are given.

The hyoscine method obviates the danger of collapse from sudden withdrawal. It saves much time and some suffering, but in my small experience I have not observed that the craving for morphine is absent at the end of the first or even of the second stage. The treatment definitely transfers the management of the case from the patient to the physician—an invaluable advantage—and thus undoubtedly enables some patients to be relieved who would otherwise prove hopeless without the aid of compulsion. But I do not think it should be considered a routine measure. It is true it has been used in a long list of cases and no fatalities are officially recorded; but hyoscine is not a drug which can be lightly prescribed. Those who intend to try the method should consult the original articles of Lott[1] and Purves Stewart.[2]

Rapid Withdrawal.—Morphine may be quite rapidly withdrawn by the aid of sodium bromide in massive doses. The alimentary canal is first thoroughly washed out by cathartics, and the daily allowance of morphine halved. Sodium bromide is then given in dram doses every eight hours. The doses are increased by 10 gr. on successive days until they reach 100 or 120 gr., *i. e.* until 300 or 360 gr. is taken in the twenty-four hours.[3] At this point the bromide is stopped, and the remaining half of the morphine tapered off during the next three days. Since the sedative influence of the bromide lasts, and even increases for some time, the period of maximum irritability resulting from withdrawal of morphine is well covered and the patient lies quiet in a semi-somnolent condition. Hot bathing and diuretics are recommended subsequently to facilitate elimination of the bromide; and later still, as the bromism weakens, mild hypnotics are required.

The treatment is entirely rational. The main source of suffering during morphine withdrawal is the grossly exaggerated condition of reflex irritability, the which is markedly reduced by the bromide salt. But it must be stated that in a few cases there have persisted, even for some months, undesirable sequelæ, *e. g.* general physical and mental debility. Such are recorded on good authority. It must not be forgotten, however, that sequelæ of the kind *may* now and then follow any method of withdrawal.

Many other methods of rapid withdrawal are advocated. One, known as the "Towns-Lambert treatment" has found numerous supporters amongst American physicians. It consists in the administration in progressively increasing doses of a "specific" composed of belladonna, hyoscyamus and xanthoxylum, together with a definite course of cathartic medication. The treatment is said to be much less violent than would appear at first sight. Its details are fully described by Dr. Alexander Lambert.[4] It is worthy of note how frequently and insistently stress is laid on the importance of free catharsis: it constitutes an indispensable item in many different plans of rapid withdrawal, and its omission is stated to involve complete failure.

Gradual Withdrawal or Tapering.—This is certainly the safest method of withdrawal and the one most usually practised, at least in this country. It is essential that the patient can afford the necessary time—and the whole of his time; for attempts at withdrawal while he continues to conduct his ordinary business are invariably futile. Furthermore, he must be *free from anxiety and worry;* and *so placed as to be unable to procure morphine surreptitiously.*

Morphine tapering differs in certain important respects from alcohol tapering. In the latter it is important to avoid any sudden large reduction during the first three or four days of treatment: in the former, it is always during these days that the largest reductions can be made. Again, while in the case of alcohol it is always easy to get rid of the smaller amounts towards the end of tapering, the exact contrary is true of morphine: there is often more difficulty in withdrawing the last grain—sometimes the last half or even quarter of a grain—than in (say) the first eleven grains.

In a few cases it is possible, without causing more than discomfort, to cut down on the first day the daily allowance of morphine to one-third: in many, to one-half; and in the great majority, to two-thirds. The only exceptions to the last reduction occur in patients who have taken the drug for many years and *who have not recently added to the daily amount;* and in those few who have themselves done some preliminary tapering before coming under treatment. Both such are probably at the time taking almost the minimum required to avoid suffering. Subsequently, each day's allowance should have a definite proportional relation to the previous day's allowance. For it does not suffice in morphinism as in alcoholism simply to subtract a regular amount per diem: roughly speaking, there should be a geometrical, not an arithmetrical, progression. But it is not possible (as it may have been on the first day) continually

[1] *Texas Medical Journal,* Nov. 1901, also *Therapeutic Gazette,* Jan. 15, 1902, p. 4.

[2] *Index of Treatment,* 1908, p. 232.

[3] Neil Macleod has given as much as 2 oz. of this drug in the twenty-four hours; I have no experience of such dosage, although I have given as much as 500 grains, and that for more than one day.

[4] *Journal of the American Medical Association,* September 25, 1909, and February 18, 1911.

to halve the allowance, still less to go on reducing by two-thirds. Probably, after the initial reduction, the most that can be accomplished with tolerable comfort is a reduction to two-thirds of the previous day's allowance. But even so, many exceptions have to be made. Whenever discomfort (which is inevitable except in very prolonged tapering) tends to pass into suffering, a halt in the reductions should be called : two or even three days may be spent on the same dose : freedom from reduction acts almost like an increase, and each succeeding day is fraught with less discomfort. Occasionally, it is good policy to give the patient a single increased dose, sufficient to free him for a time (say one night) from all abstinence symptoms. After such a rest, he will probably face the succeeding reductions with fresh courage.

The object of the plan outlined is to ensure a *continually diminishing decrease as the dose becomes smaller*. This is essential, for in every case a stage is ultimately reached at which each reduction is of very real moment. Whenever time is of no importance the tapering of the last three quarters, half or quarter of a grain should be carried out very slowly indeed. The final injection should not exceed $\frac{1}{40}$ gr. At this stage in the treatment, the patient as a rule can detect a slight but very short-lived euphoria even from this amount. With tapering carried out to this extent, all but slight discomfort may be avoided, and, what is true of no other method, the physical health begins to improve *before* final withdrawal. Moreover, the use of all adjuvant drugs can then be sometimes dispensed with.

Usually, of course, such prolongation of tapering is impossible. Then it is necessary to employ other drugs towards the end. A modification of the sodium bromide method, already described, is often very successful; or a single full hypnotic injection of hyoscine may be given every night. Or, again, these two drugs may be used together, the bromide being given during the day, the hyoscine at night. An attempt may sometimes be made to keep the patient asleep during the greater part of the day as well as during the night; but this is not often successful, and it is objectionable on other grounds. There are two important points in the use of hypnotics: (1) Full doses are necessary—hypnotics which fail to give sleep, always do harm; and (2) the use of hypnotics should be put off as long as possible in the tapering course; indeed, it is best to defer them until the end of the course is clearly in view.

Although abstinence symptoms may be avoided simply by a sufficient prolongation of the tapering, yet lack of time commonly precludes this course. Resort must then be had to drugs and other therapeutic measures. Dyspepsia yields to bicarbonate of soda, with careful dieting. For nausea and vomiting, a good plan is medical washing out of the stomach with warm alkalinised water. Sweating is promptly checked by small hypodermics of atropine ($\frac{1}{100}$ gr.), which may be added to the morphine injections. Muscular restlessness is relieved by friction and hot baths, which latter are useful for most abstinence symptoms. A mild imitation of morphine euphoria sometimes follows nitroglycerine, which certainly relieves the general vaso-constriction and chilliness of the skin so frequently observed. Caution must be employed with this drug in that it is sometimes thought capable of itself setting up a habit. Strychnine should never be given until after all morphine has been finally withdrawn : it undoubtedly intensifies the abstinence symptoms.

There is a danger in giving large doses of morphine hypodermically which is not often mentioned. Most morphinists have at times accidentally made an injection into a vein : the accident is shown by the absence of the usual tumour at the site of the injection. If the injected dose is large, the ensuing symptoms which come on instantaneously are extremely severe. They resemble the result of a large inhalation of amyl nitrite : there is a violent and extensive vaso-dilation, most marked in the head and face, which latter becomes a deep crimson. The sensation is terrifying in the extreme (the patient feels on the verge of a fit), and I have a suspicion that sudden death has occurred more than once.[1] The accident can be avoided by distributing the larger injections, either by making several punctures, or by injecting through the one puncture at several different levels.

It has been advised in the treatment of hypodermic morphinism to abandon the needle and substitute morphine by the mouth or rectum. But I am inclined to think that the disadvantages of the change outweigh its advantages. It is a disadvantage to be obliged to double the dose or nearly so; and, absorption from any part of the alimentary canal being so much more variable than from the subcutaneous tissue, there arises an increased difficulty in gauging the physiological influence of each individual dose. It is, I think, preferable to continue the method initiated by the patient. Moreover, there seems some gain in continuing the number and time of injections used by the patient. This, however, is often impossible in practice. And on the average three or four injections in the twenty-four hours given at approximately equal intervals should suffice.

It has been considered a good plan to inform the patient of each reduction made in dosage,

[1] Cases of sudden unexpected and unexplained death have been recorded several times in morphinism.

and so encourage him to take an interest in his progress. This may be advisable in some cases, but it certainly is not in the majority. Indeed, most patients, if questioned on the point, express their wish to remain in ignorance of their dosage; and I have rarely told a patient the amount he was taking without regretting it: quite often an immediate increase in the severity of his abstinence symptoms has followed the information.

For injections, the all-glass syringe should always be used. Subcutaneous abscesses are an irritating complication in new cases: they are usually ascribed to a dirty needle, but they are almost unknown in the case of those who restrict themselves to the above syringe—a fact which suggests that the plunger rather than the needle was the chief source of infection.

Treatment following Complete Withdrawal of Morphine.—A few days after the final withdrawal of the drug—the exact number varying with the duration of the tapering and other circumstances—all abstinence symptoms disappear, often so suddenly that the patient can fix almost the hour of their disappearance. He then begins to experience sensations of well-being to which he has long been a stranger. It is as if a permanent cloud had suddenly been lifted. He awakes feeling *fresh*, he begins to enjoy his meals: his interest in daily events comes back, and physical exercise, previously regarded as a duty (if taken at all), begins to appeal to him as a pleasure. Unfortunately, all this does not continue without interruption. As in alcoholism, so here, there are recurring days on which the craving for drug euphoria returns; but in the case of morphinism these intermittent cravings are more severe, longer in duration, more frequent and more persistent. Until they have finally ceased, the patient is not free from the danger of relapse, though this danger is a progressively diminishing one. Obviously, then, the patient should remain under observation, supervision and treatment for a period which depends on many circumstances. Some of these circumstances may be stated in the order of their relative importance: (1) the temperament of the patient; (2) the duration of his addiction to morphine; (3) the maximum dose to which he had attained; (4) the number of his previous relapses; and (5) his domestic environment. The drug which is most useful at this stage is in my opinion strychnine, given hypodermically in full doses.

Prevention of Morphinism.—Though undoubtedly increasing, morphinism is not yet very common in this country. Quite half of the cases occur in medical men, their wives and near relatives, and in hospital nurses, dispensers and chemists. In the remainder, with few exceptions, the habit has been initiated through medical prescription. Now, the essential factor in all cases is the disastrous knowledge and remembrance of the fascinating euphoria induced by the drug. Than morphinism we could find no better illustration of the old proverb which reminds us of the folly of wisdom in certain circumstances. For it is a fact that forgetfulness of euphoria is too frequently unattainable. Vivid remembrance is prone to arise unbidden and force itself on the consciousness in every emergency fraught with stress or worry, or even under conditions involving mere slackness or boredom. Obviously, a grave responsibility devolves on the physician who prescribes such a drug; one can conceive no greater cause for remorse than to have administered to a morphinist his first enlightening dose when other and less dangerous measures would have sufficed. And yet there can be no question that the drug is still frequently ordered without adequate justification: a well-known physician has long prescribed it in the hypodermic form as a routine treatment for sciatica.

We cannot do without morphine: its power of subduing pain and of inhibiting intestinal peristalsis—these alone would render it essential. But many precautions can be taken. It should be superfluous to say that no patient should ever be taught to handle the hypodermic syringe. Morphine should never be given hypodermically when mouth administration will suffice. And, further, morphine (or indeed opiates of any kind) should never be given even by the mouth when a less treacherous drug can be substituted. For example, it should never be given for mere insomnia: it is, at any rate, but a poor hypnotic.

I see no reason why a prescription for morphine should ever be written at all: in this tablet and tabloid age the drug can always be carried and directly supplied by the physician, even by one who does not dispense: this would actually involve less time and trouble than writing a prescription. Nor does there seem to me any justification for ever mentioning the name of the drug in the sick-room or consulting-room: the necessity for silence on this subject should be impressed upon the nurse in charge of the case. Of a certainty many cases could have been prevented by this simple precaution.

From the standpoint of avoiding a euphoria likely to make an abiding impression on the patient's memory, dosage is all-important. When it becomes really necessary to give an opiate, the dose should be sufficiently large to include sleep amongst its effects. The most dangerous doses are those which just fall short of producing sleep. Many morphinists have traced the formation of their habit to opiates which, sufficient to relieve pain, have afforded them several wakeful hours of extreme happi-

ness. Indeed, not a few have confessed to me that in these circumstances they have designedly forced themselves to remain awake, in order not to miss any of the pleasurable sensations resulting from their dose. It should be the rule, therefore, to give frankly hypnotic doses, or, perhaps better, to combine with the opiate some purely hypnotic drug, *e.g.* hyoscine or veronal.

The danger of setting up a habit by opiates, especially by morphine injections, is probably more urgent in the case of alcoholists than in any other class. Hence extra precautions are demanded. In the Norwood Sanatorium (except, of course, in morphinists) morphine is used only in rare emergencies, and then never by itself. The drug usually given in combination in the one injection is apomorphine, and that for two reasons: (1) apomorphine in emetic doses is usually itself indicated, and (2) the addition of this drug in nauseating and rapidly hypnotic doses effectually conceals the more enduring euphoric influence of morphine. It is unnecessary to add that the name of the drug (morphine) is never mentioned.

I am inclined to think that the general adoption of the above and similar precautionary measures would do far more to prevent the growth of morphinism than can ever be effected by prohibitive legislation in this country.

Perhaps it is fortunate that morphinists rarely become pregnant, the habit involving in nearly all cases a temporary amenorrhœa and sterility. Yet pregnancy may occur. Then there arises a nice question as to the best course to pursue. On the one hand, withdrawal is exceedingly liable to cause abortion, in which case the child will be sacrificed: on the other, the infant is certain to be born a morphinist (congenital morphinism) with probably a high, but unknown, tolerance of the drug already established, in which case very difficult questions of treatment, especially as regards dosage, will have to be faced. A patient of mine found herself pregnant while taking 15 gr. of morphine a day. She underwent a very gradual tapering course, with the result that she gave birth at full term to an infant normal in all respects. Such is probably the best course to adopt.

Cocainism

Cocainism seems more directly destructive of both mind and body than any other drug habit. Fortunately it is rare in this country, at any rate in its pure form. But it is not uncommon for morphinists to add small doses of this drug to their morphine injections: the addition is said to "bring out the mental flavour" of the morphine.

As to whether cocaine should be suddenly withdrawn or cautiously tapered off, there is a marked diversity of opinion. For example, K. C. Drury says: "Decocainisation should be by the gradual method. . . . Any attempt to suddenly withdraw it or very largely reduce the quantity is likely to be followed by alarming symptoms, mental and physical, mania and collapse."[1] Whereas T. D. Crothers lays it down that "Abrupt withdrawal of the drug is the safest plan. . . . In the method of gradual withdrawal it has been found that small doses may result in collapse.[2] The two views are impossible of reconciliation. I can only refer to my own experience, which, however, is small.

In those cases in which the drug in small quantities is added to morphine injections, I have always at once withdrawn all the cocaine. No bad result has ever followed: the patient has simply said he missed it. In the few cases of pure cocainism treated by me, I have in all withdrawn the drug by very rapid tapering in from two to three days, no matter what the amount that was being taken. In no case was there more than discomfort: nothing remotely resembling collapse ever occurred. In one case only there followed a mild nocturnal delirium for a few days; but this may have been due to a septic condition: there were numerous abscesses in the site of old injections and an evening temperature of 101° F.

I was encouraged to adopt such rapid withdrawal by a fact disclosed in the histories of all these patients. On more than one occasion they had through inadvertence been without their accustomed cocaine for periods varying from twelve to thirty-six hours, and had confessed that no serious suffering ensued. This is in sharp contradistinction to what happens in the same circumstances with morphinists. Also, it is a fact that, unlike morphinism, cocainism not very rarely exists in an intermittent form.

The special methods of rapid withdrawal of morphine—the hyoscine and sodium bromide methods, already described—are practicable in cocainism.

But if the withdrawal of cocaine is relatively easy, the very opposite is true with regard to the prevention of relapse. Relapse into cocainism is exceedingly common, according to some, inevitable. Whether this be due to the extreme fascination of the cocaine euphoria or to the mental degeneration which so quickly sets in, or to both, it is obvious that the supervision after withdrawal must be prolonged and careful if the patient is to have any chance of permanent freedom from the drug.

Other Drug Habits

All that has been said of the treatment of hypodermic morphinism applies, with the

[1] Green's *Encyclopædia of Medicine and Surgery*, Part XV, p. 451.

[2] *The Disease of Inebriety*, 1893, p. 360.

obviously necessary modifications, to those drug habits in which the essential factor is a morphine or opium euphoria—to morphine taken by the mouth, opium eating and smoking, laudanum and chlorodyne drinking, etc. All may be tapered off under supervision according to the general principles laid down under morphinism; and, other things being equal, it may be said that the process here is comparatively easy and fraught with less discomfort. Also, any of these drug habits, if deemed sufficiently severe or in special circumstances, may be treated by rapid withdrawal under the sodium bromide or hyoscine methods.

Chloral has long been known as a habit-forming drug; tolerance is established, and there is intolerance of sudden withdrawal. Chloralism closely resembles chronic alcoholism as regards its chief abstinence phenomenon. Sudden withdrawal in a patient who has acquired high tolerance may give rise to a typical attack of delirium tremens,[1] even in total abstainers from alcohol. Moreover, as in alcoholism, the attack begins about three days after withdrawal, and in favourable cases lasts just about the same time, namely, three or four days, ending in the crisis of sleep. Hence, in the treatment of chloralism cautious tapering on the alcoholic model is the best mode of withdrawal. It is stated that chloral delirium tremens is especially dangerous on account of the fatty degeneration of the heart caused by the drug.[2]

The comparatively modern hypnotics, trional and veronal, are now known to be capable of starting drug habits. Both drugs establish tolerance, which involves intolerance of sudden withdrawal. The most marked signs of tolerance are a peculiar anæmia and muscular inco-ordination shown by an ataxic gait. In the case of the veronal habit, at any rate, the chief abstinence phenomenon is the same as in chronic alcoholism and chloralism, namely, an attack of delirium tremens, commencing at the same interval following withdrawal, indistinguishable in its symptomatology, and lasting approximately the same time.[3] Hence the necessity of cautious tapering. F. H.

FOOD POISONING

Food poisoning may arise from most articles of diet. There exist several methods by which poisoning may occur, and a certain knowledge of these is necessary for undertaking the treatment. Thus considering meat poisoning as a type there may be the following causes—

1. **The Animal may have been Diseased during Life.**—The bacteria causing this may continue to live in the flesh subsequent to slaughtering. Such bacteria commonly belong to the "typhoid-coli" group and fall into two main sub-groups represented by (1) B. enteritidis of Gærtner and (2) B. suipestifer. The B. suipestifer is identical with the organism occurring in hog-cholera or swine-fever. Bainbridge has shown by absorption experiments that food poisoning formerly ascribed to B. paratyphosus (Type B) is probably due to B. suipestifer. These organisms can sometimes, with due precautions, be grown from the meat and also from the stools of the infected persons, these individuals, therefore, being infectious to others. It is possible that in some cases due to such bacterial disease of animals the bacteria are not present in the meat consumed, but only the toxins produced by them.

Articles affected in this manner may show no change of colour, smell, or condition, and the presence of the organisms can only be proved by bacteriological investigation. Even thorough cooking is usually insufficient to render such meat safe. The great majority of all epidemics of food poisoning fall into this class and the percentage of satisfactorily proved cases increases with the employment of modern bacteriological methods.

2. **The Meat may become Diseased or Putrefied subsequent to Slaughtering.**—Certain bacteria may infect it, especially B. proteus and B. coli. Meat infected by B. proteus may have an unpleasant smell. Thorough cooking, but not smoking, usually renders it no longer poisonous. When the organism is B. coli there are no signs. It is possible that B. proteus and B. coli are signs of contamination rather than themselves the cause of poisoning.

These two groups comprise the majority of outbreaks of food poisoning, including those due to canned foods. Formerly great stress was laid on "ptomaines." These are alkaloids of animal origin, and are of simple chemical structure. It is now believed that they are of little importance. A few poisonous fungi may act by virtue of alkaloids, but even in their case such action is doubtful.

Canned foods were formerly considered to be dangerous, owing to the risk of metallic poisoning, but the results are more often due to bacterial infections. Various parasites, such as trichinella spiralis or certain tape-worms, may be present in food and lead to infection. The treatment of these conditions is dealt with elsewhere.

The diagnosis of food poisoning usually depends on a number of persons, who have taken food from a common origin, being attacked by similar symptoms. In some cases it can be traced when a single individual has had an unusual article, such as mussels. It must be

[1] *On Alcoholism*, Francis Hare, 1912, p. 121.
[2] Cushny, *Textbook of Pharmacology*, Fourth edition, p. 192.
[3] *On Alcoholism*, Francis Hare, 1912, p. 122.

remembered that idiosyncrasy to various substances is very common, and many people are upset by a mushroom harmless to others. Cases where the disturbance can be ascribed to idiosyncrasy are rarely severe.

The treatment is considered under the following groups—

1. **Meat Poisoning.**—Beef, veal and pork are most often to blame. Mutton rarely causes poisoning.

The symptoms in an outbreak will appear in different cases after varying intervals, commonly in four to six hours, and once commenced, tend to progress rapidly. The onset occurs with nausea, vomiting, abdominal pain and diarrhœa with yellow motions.

When a case with a rapid onset is seen early the first step is to ensure that the stomach is emptied. A tube should be passed [1] and the stomach well washed out. As these poisons do not corrode the mucous membrane, this can be done without risk. In the absence of a tube, an emetic should be given.

In cases of food poisoning it is unnecessary to oil the tube.

When an emetic has been given it is important that vomiting should occur. If it does not follow shortly repeat the emetic or give one of the others. There is no reason against giving two or three consecutively. Do not wait more than half an hour.

These measures to empty the stomach should be employed even in the presence of vomiting.

The next step is to administer a brisk cathartic, the best being castor oil, giving 2 oz. to an adult. This ensures rapid passage through the intestines.

Even in early stages the pulse is commonly weak, and collapse marked, and stimulants should always be administered. Brandy is especially useful and should be given in full doses, for an adult 2 oz. should be given at once and repeated at intervals of a few hours. (It may be noted that in many cases of food poisoning those persons who have drunk wine have escaped lightly.) Strychnine $\frac{1}{30}$ gr. may be injected hypodermically. The patient must be kept in bed absolutely, and wrapped in warm blankets with hot-water bottles if there is any tendency to collapse.

The comfort of the patient may be helped by giving ice to suck and applying hot fomentations to the epigastrium and abdomen.

The diet at this stage need not be considered, as the patient can safely be starved for twenty-four hours. In any case solids should not be given.

Water should be given at all times when asked for, but a limit of 4 oz. for an adult should be placed on the amount taken at one time if the patient shows a tendency to gulp down large quantities.

If severe vomiting persists, and is causing exhaustion, the stomach should again be washed out.

In many cases the symptoms last but a few hours. The patient should not be allowed to get up for several days until all signs of weakness of the pulse and abdominal disturbance have disappeared. The diarrhœa is at first of service in ridding the body of the poisons, but as the condition advances it may become frequent and ineffectual, and attempts must be made to check it. Pulv. Cretæ Aromaticus cum Opio in doses of 40 gr. may be employed. (Tablets should never be given whole, but must be crushed to powder.) If vomiting prevents the administration of drugs by the mouth, or if the diarrhœa continues, a starch and opium enema should be given. For this two teaspoonfuls of starch are added to 5 oz. of water and the mixture heated just to boiling with constant stirring. The heating is continued for ten minutes and then the mixture is cooled and $\frac{1}{2}$ dr. of tincture of opium added. The enema is given cold through a gum elastic catheter (No. 12) with a glass funnel, and a pad of wool or lint should be pressed against the anus to aid retention of the enema.

In some cases purging arises very rapidly and severely. Castor oil must be omitted and opium given. If the vomiting and purging is extreme, morphia should be injected hypodermically.

If the symptoms have continued for a day or two, the conditions which particularly call for treatment besides the above are the diminution of the fluids of the body and the general collapse. If the skin becomes inelastic, a long rectal tube should be passed and tepid (not hot) water allowed to run in by syphon action from a height of 12–18 inches. For this the patient is turned on the left side with the buttocks slightly raised by placing a pillow below. A pint at a time should be run in if possible.

As stimulants, strychnine $\frac{1}{30}$ gr. every four hours should be injected hypodermically for twenty-four hours, and brandy given by the mouth.

The diet should be confined to milk until convalescence has set in.

Such is the treatment in cases with an acute onset and a short duration. Convalescence is usually slow.

In other instances, even with an identical origin, the onset may be slower and less acute, and the illness more prolonged, or after an acute onset the more severe symptoms may subside, and yet convalescence does not set in. Now, it has been mentioned that the organisms

[1] The preparation of emetics, and the method of passing the stomach tube, is described in the article on *Metallic Poisoning*.

commonly present in meat of diseased animals are B. enteritidis of Gærtner and B. suipestifer. Both these belong to the typhoid-coli group and may produce an illness closely resembling typhoid fever. Infection with Gærtner's Bacillus commonly results in the rapid onset of an acute attack resembling that described above. The conditions produced by B. suipestifer may be distinguishable from typhoid fever only by the agglutinating power of the serum of the patients to the various organisms and by absorption tests. Hence the illness may follow a typhoidal course either from the onset or subsequent to the acute symptoms when infection has occurred with the two types of organisms simultaneously. Such cases must be treated in the same manner as typhoid fever. It is important to note that the organisms may be excreted in the motions, which must, therefore, be treated with the same care as in typhoid fever. It is wise to take such precautions from the onset.

2. **Poisoning by Fish, Mussels, etc.** (a) *Fish Poisoning.*—The flesh of certain fish is poisonous. These are generally known and avoided. Fish poisoning is sometimes due to the fish having been kept too long and becoming infected with bacteria, especially B. proteus and B. coli. Other organisms such as B. enteritidis sporogenes may also occur. Some outbreaks have been due to organisms of the typhoid-coli group. The course and treatment of such conditions is similar to that given under Meat Poisoning.

(b) *Mussel Poisoning.*—The danger in eating mussels is considerable. The cause is yet uncertain but is connected with sewage contamination. Various organisms, including B. coli, streptococci and B. enteritidis sporogenes, have been isolated from mussels, but the clinical symptoms usually present suggest that these are not the direct cause of the poisonous effects. The symptoms usually appear with extreme rapidity, often within ten minutes of the meal, and the patient may be completely collapsed in half an hour. There is dizziness, dyspnœa and collapse, and the pulse becomes soft and very rapid. Either at this time or later intolerable itching and various cutaneous phenomena, such as urticaria, develop.

The patient must be put to bed and wrapped in warm blankets with hot-water bottles. Pass the stomach tube and wash the stomach repeatedly with large quantities of fluid. When the washings are clear, leave castor oil (1 oz.) in the stomach. In the absence of a stomach tube give emetics. Give stimulants freely: brandy in 2 oz. doses, or spirits of ether 1 dr. by the mouth, or ether 30 min. hypodermically. Inject atropine sulphate $\frac{1}{50}$ gr. hypodermically.

Recovery from the acute symptoms usually occurs within twenty-four hours, but some weakness remains for a few days.

In some cases gastro-enteritis may follow or be present from the commencement. The treatment described under meat poisoning should be followed. There is evidence that outbreaks of typhoid fever have been due to mussels, even when typhoid bacilli have not been isolated.

(c) *Poisoning through Oysters, Crabs and Lobsters.*—Several outbreaks of typhoid fever have been traced to oysters. Apart from this, oysters spoil readily and produce gastro-enteritis. Crabs and lobsters often cause gastric disturbance. Children suffer more than adults. The symptoms are often mild, but an emetic, castor oil and brandy should be administered. If severe, the stomach should be emptied, and measures carried out as described under Meat Poisoning.

3. **Mushroom Poisoning.**—There is a marked idiosyncrasy to mushrooms, many individuals being unable to consume safely even the "edible" varieties. Children especially are often affected. Poisoning, however, usually results from the ingestion by mistake of non-edible varieties. The cause of the poisoning is not yet understood. From some non-edible mushrooms the alkaloid muscarine has been isolated. The symptoms cannot be entirely ascribed to this.

In many cases mushroom poisoning has the ordinary symptoms of a gastro-enteritis, and for these the treatment described under Meat Poisoning should be followed. The washing of the stomach must be done repeatedly, as pieces of fungi often adhere to the wall.

In other cases the symptoms suggest a nervous origin. Excitement or delirium, resembling that of alcohol, occur together with disturbance of vision and pulse, and at times purging and diarrhœa. Such symptoms may be due to muscarine or other alkaloids. Except in the presence of delirium, a hypodermic injection of atropine $\frac{1}{50}$ gr. should be given. Otherwise the treatment should be the same as for the diarrhœal form.

4. **Poisoning through Canned Foods.**—Canned food may lead to poisoning owing to the action of the acids in the juices dissolving the tin or lead. This is most liable to happen in cases of fruits or vegetables. It is a rare form. Poisoning is more often due to organisms present, and the course and symptoms resemble meat poisoning. Similar treatment should be adopted (*vide* Meat Poisoning).

5. **Ice-Cream.**—Very poor ingredients are sometimes used for ice-creams sold in streets, and poisoning may result from a variety of causes. Vanilla ice-cream has caused several outbreaks. The symptoms are commonly those of gastro-enteritis and should be treated on the lines given for meat poisoning.

6. **Cheese.**—Poisoning by cheese was formerly

ascribed to an alkaloid tyro-toxicon, but probably is usually bacterial. Symptoms: Gastro-enteritis. Treatment: As for meat poisoning.

7. **Milk.**—Milk may become infected in various ways. Certain organisms present in an animal may pass into its milk. Dairymen and others handling the milk may infect it with diseases from which they are suffering or of which they are carriers. Tuberculosis, typhoid, diphtheria and other conditions may be spread thus. Apart from this, milk is usually given every opportunity of becoming a suspension of bacteria, some of which are responsible for much of the "summer diarrhœa."

8. **Specific "Sausage Poisoning"** (*Botulism*).—Almost confined to Würtemberg. Due to an anærobic bacillus (B. botulinus). Symptoms: Paralysis of cranial motor nerves. Treatment: Wash out stomach. Emetics. Stimulants. An antitoxic serum has been prepared in Germany and should be tried. H. L. T.

AUTO-INTOXICATION AND INTESTINAL INTOXICATION

We have travelled far since the days when Bouchard thought that he could detect the existence of an auto-intoxication by the simple device of comparing the toxicity of a suspected urine with that of a normal individual. For we now realise that to inject into an animal's circulation fluids differing widely in osmotic pressure from its blood gives most erroneous results. At the present time the application of the term **"auto-intoxication"** has become much restricted; intestinal intoxication resulting from bacterial changes should certainly not be so described. Strictly speaking, the term is only applicable to conditions where a metabolic defect results in the setting free of a substance which produces toxic symptoms. The clearest examples of these are to be found among the "inborn errors of metabolism," as they are called by Garrod. Apparently they are due to the absence of some specific ferment, so that some substance which would otherwise have been completely resolved into urea, carbon dioxide, water and the like passes into the circulation and ultimately has to find its way out in the urine. *Cystinuria* is a good example. Here the sulphur-containing amino acids formed from the breakdown of the proteins of the tissues give rise to hexagonal crystals in the urine, which may, if infection of the urinary tract occurs, give rise to a calculus. But even here it will be noted than an extraneous infection is necessary before the patient suffers any real inconvenience (see article on *Renal Calculi*). *Alkaptonuria* is another example. Here the tyrosin of the protein molecule gives rise to a substance which reduces Fehling's solution and also turns the urine brown on standing. The chief inconvenience from this is that the patient is likely to be rejected for life insurance, although the reducing substance is not sugar and is harmless. But there may also be some ochronosis or pigmentation of the sclerotics and cartilages and a peculiar form of chronic arthritis producing a characteristic "goose gait." Unfortunately we have at present no way of producing a proper breakdown of the tyrosin which is responsible for this curious condition. *Pentosuria* is another inborn error of metabolism in which the urine contains a sugar derived from the carbohydrate fraction in the nuclei of the cells. The condition is a harmless one, and is very rare. Again, the principal inconvenience it entails is the liability to rejection for life insurance. Failure in the breakdown of the purin groups in nucleo-proteins is usually not congenital, though the tendency to it may be hereditary. How far *gout* is to be regarded as an auto-intoxication due to this is discussed in the article on that subject. The best example of an acquired auto-intoxication due to altered breakdown in the protein molecule is *uræmia*, for the treatment of which the reader is referred to the appropriate article. This exhausts the list of auto-intoxications which can definitely be referred to the simple or compound proteins.

Auto-intoxications resulting directly from carbohydrate metabolism are very few. *Lactic acid* is formed whenever the oxidation of carbohydrates is incomplete. The principal symptom produced is dyspnœa, and it may be presumed that this dyspnœa follows on the stimulation of the medullary centres by the acid. The normal stimulant to the respiratory centre is CO_2, and if it is not present in sufficient quantities apnœa results. This soon causes some degree of oxygen starvation with consequent formation of lactic acid. The dyspnœa which results must therefore be regarded in part as a compensating mechanism for the absence of the normal stimulant. Unlike other incomplete oxidation products, lactic acid can be got rid of by inhalations of oxygen. The chief symptom it produces is muscular fatigue, affecting the striped muscle, causing cramps therein, and the cardiac muscle causing dilatation of the right heart. It may be noted that a mixture of oxygen with 4 per cent. of CO_2 will be more effective than pure oxygen, because it will continue to provide the stimulant to normal respiratory effort. Only a tentative beginning has been made with such a mixture in the treatment of Cheyne-Stokes respiration; but, as pointed out by Cushny, it is probable that such a mixture would also be useful in opium poisoning.

Oxaluria may result either from ingestion of oxalates in the food, or from fermentative

changes in the carbohydrates in gastritis or chronic pancreatitis. It is perhaps, therefore, not strictly an auto-intoxication, since the changes are presumably due to microbes. The symptoms it may give rise to and their treatment are described under *Renal Calculi*.

Of all the abnormal acids the most striking one is diacetic acid, because of its easy detection by ferric chloride or by nitro-prusside of soda and ammonia. To the former reagent it yields a claret colour, and to the latter the tint of a solution of permanganate of potash. Although it is chiefly met with in diabetes it is only indirectly due to the failure of carbohydrate metabolism, owing to the consequent incomplete oxidation of the fats and the amino-fatty acids of the protein molecule. It is a decomposition product of a fatty acid, oxybutyric acid, and in its turn may decompose into acetone. It is seldom produced in sufficient amount to cause symptoms in any other condition than diabetes. The term *acidosis* implies its existence, and *acid intoxication* its occurrence in sufficient amount to produce a toxic effect. It is also met with (*a*) under all conditions of starvation such as rectal "feeding," new growth of the œsophagus and the like; (*b*) incomplete oxygenation such as occurs in broncho-pneumonia and mountain sickness; (*c*) certain toxic conditions of the liver, such as cyclical vomiting of children (which generally seems to be the result of a B. coli infection), pernicious vomiting of pregnancy, phosphorus poisoning, and post-anæsthetic poisoning. For the detailed treatment of these conditions, reference must be made to the appropriate articles. Here it is sufficient to say that, as in diabetes, the most important part of the treatment is to prevent further formation of these acids by getting sugar assimilated by the tissues and to neutralise such acids as have been formed by the free administration of alkalis. To these ends, if food cannot be retained by the stomach, 5 per cent. of dextrose in normal saline must be given *per rectum*, while mixed alkalis must be given in the doses and by the methods described under *Diabetic Coma*. It will, of course, be understood that in diabetes levulose must be substituted for dextrose in the rectal salines. In the cyclical vomiting of children the first sign of an attack, such as a furred tongue, offensive breath, and white stools call for small doses of grey powder or calomel. Food had better be restricted to barley-water and arrowroot.

Intoxications resulting from deficiencies, either in the diet or in the defensive activity of the ductless glands, are perhaps scarcely to be included in the auto-intoxications; but it may be well to point out here that scurvy, beri-beri, and perhaps some other forms of polyneuritis may be set up by the absence of basic substances from the diet to which the name of vitamines has been given (see article on *The Dietetic Factor in Treatment*).

It is inevitable that in a work on treatment, an article on auto-intoxications must largely take the form of cross-references to articles on diseases of those organs in which the intoxication arises or produces its effects.

Intestinal intoxication is diagnosed with great frequency to account for otherwise inexplicable conditions. It is important, however, that we should have definite grounds before coming to such a conclusion. Normal inhabitants of the bowel, by straying beyond their proper limits, may produce definite infections; thus, the B. coli may set up cystitis, pyelitis, cholecystitis, or phlebitis; and the streptococcus fæcalis can ingraft itself on to heart-valves damaged by rheumatism. Or the body may fail to neutralise the soluble poisons produced by bacteria, and an intoxication may result. There are three main lines of defence against a microbe and its toxins; the resistance of the intestinal epithelium, the bactericidal properties of the blood and the antitoxic functions of the liver and ductless glands.

The infant starts with a sterile alimentary canal, but speedily acquires bacteria therein, chiefly organisms derived from the skin of the mother's nipple. In the intestine of bottle-fed children there are many more organisms of the B. coli class. As childhood goes on, the flora of the intestine becomes large and varied. Proteins putrefy, carbohydrates ferment, and to some extent these two processes are antagonistic. Putrefaction is the disadvantage of a large intestine, the advantage being the absorption of water by which the bulk of the fæces is greatly reduced, so that the bowel need not be emptied normally more than once a day. There is also less need for drinking fluid. Some extremists appear to think that it is better to dispense with the colon altogether than to possess an indolent one. But we can hardly suppose that the colon would have been evolved without a compensating protective mechanism. Putrefaction mainly affects the aromatic and sulphur-containing groups in the protein molecule. The sulphates set free are conjugated in the liver with the aromatic products to form ethereal sulphates which are practically harmless. The best known of these is indican. This illustrates the way in which the body reacts against intoxication, but it must be pointed out that there may be a large formation of ethereal sulphates with merely a trace of indican, while there is some evidence that indican may be formed within the body apart from these putrefactive changes. Merely examining the urine for indican is, therefore, not a

satisfactory method of diagnosing intestinal intoxication. We may have here also an explanation of the comparative failure of the phenol compounds as intestinal antiseptics. By combining with the sulphates they deprive the body of the power of rendering harmless those putrefactive substances the formation of which they cannot altogether prevent. It helps us further to understand the value of sulphates in certain intestinal diseases. They are not only aperient but antitoxic.

The following types of intestinal intoxication have been recognised—

1. *Indolic* due to the B. coli and perhaps the B. putrificus. The commonest form is seen in marasmic children with a distended abdomen and chronic intestinal indigestion. The subjects are sharp-witted, intolerant of cold and easily fatigued. Carbohydrates are not well digested. There is a marked increase in the indican and other ethereal sulphates in the urine. As for treatment, the carbohydrate should be restricted to well-cooked rice and biscuits. Milk should be peptonised for a time, and a moderate amount of finely divided meat given. Gelatin may be useful because it contains no tryptophan, the precursor of indol. A few rather generous meals are better than frequent feeding. High irrigation of the bowel may be beneficial.

2. *Butyric* chiefly due to B. ærogenes capsulatus. The bacterial action sets free nascent hydrogen, which causes much reduction of the bile pigment, so that there is an excess of urobilin in the fæces and urine. Addition of a strong solution of mercuric chloride to the fæces produces a red colour, rendered more distinct by subsequently throwing them into water. There is little or no indican in the urine. Indefinite invalidism may be the chief symptom. The patient is often sour-smelling, the epithelium of the tongue and mouth is seen to be desquamating. Hence the irritable condition of the alimentary canal with the tendency to diarrhœa. Anæmia supervenes owing to the hæmolytic action of the toxins found in the bowel. The treatment should be on the general lines described below.

3. *Combined Indolic and Butyric.*—In this, nervous symptoms occur early. The outstanding features of the case are mental depression and muscular fatigue. The subjects become invalided more rapidly than with either of the former types occurring separately.

4. *Carbohydrate Fever.*—It is not clear how far this type coincides with the fermentative type described under (2). It is certain, however, that rigid restriction of the carbohydrates in the diet leads to marked improvement, while carbohydrate excess may cause an exacerbation of symptoms.

5. *Sulphæmoglobinæmia.*—A curious form of cyanosis has been found to be due to the presence of sulphæmoglobin in the red corpuscles of the blood. Lately Mackenzie Wallis has found a nitrifying bacillus in the saliva in these cases. The nitrites reduce oxyhæmoglobin after absorption from the intestines, and sulphuretted hydrogen can then readily form sulphæmoglobin. Great benefit has been derived from the removal of all infected teeth, administration of an autogenous vaccine prepared from the organism in the saliva, and the free use of saline aperients.

6. *Methæmoglobinæmia* is less common, and, no doubt, several of the cases so described have really been ones of sulphæmoglobinæmia. In this condition there is also cyanosis, but the spectroscopic appearances of the blood are different. It may also be brought about by the habitual use of coal-tar drugs. Avoidance of all such drugs, a rigid milk diet and insoluble intestinal antiseptics are the main points in treatment. There is usually diarrhœa, which may also have to be treated.

7. *Pressor Diamines* have been discovered in the bowel by Barger, Walpole and Dale. They are, no doubt, responsible for the rise of pressure which frequently occurs in later life without obvious cause, especially in constipated persons. The treatment is that described under the prophylactic measures in chronic interstitial nephritis (*q. v.*) in addition to the ordinary methods.

The general scheme of treatment suitable in cases of proved or suspected intestinal intoxication is as follows—

1. *Avoidance of Putrefactive Contamination of Food.*—All food should be cooked as far as possible. Cheese, especially the riper varieties, should be avoided, as should high game. All fruit should be peeled. Careful attention must be paid to the teeth, since anærobic bacteria which lurk in the interstices are a great factor in intestinal putrefaction.

2. *Promotion of Prompt Digestion and Absorption.*—Here again attention to the teeth is important to allow of proper mastication. Hydrochloric acid should be given if it is deficient in the gastric juice. But in the cases of butyric fermentation diastatic ferments such as Taka-diastase are better than hydrochloric acid, which is not well borne. Pepper, mustard, excess of salt, vinegar and lemon are irritant to these patients. Demulcent drinks are indicated. The butyric type need careful preparation for a generous diet. Emotional irritability or mental depression, increase in the ethereal sulphates of the urine, of gas-producing bacilli in the stools, or of intestinal flatulence are signs that the food should be reduced. Intestinal flatulence indicates reduction

in the amount of carbohydrates. If there be atonic dilatation of the stomach, lavage should be employed. Rest after meals should be enjoined.

3. *Limitation of the Number of Bacteria.*—Though it is obviously impossible to render the intestines sterile, the number of bacteria can certainly be considerably reduced. Calomel in small and divided doses followed by a saline purge next morning is a time-honoured method of attempting to effect this. However useful this may be to start treatment, we must beware of a routine use of strong purgatives, for, by removing the superficial epithelium of the bowel, they may facilitate septic absorption. After a preliminary dose of calomel, my custom is to give 3 min. of Cyllin Medical in capsules three times a day for not more than four days. If continued longer than this, I think it is apt to cause irritative symptoms. After that naphthalene tetrachloride in 5 or 10 gr. doses should be given three or four times a day. As it is insoluble and cannot, therefore, be absorbed, it does not produce any toxic symptoms. Salol has not been a success, but cachets of β-naphthol in 5 gr. doses sometimes give good results. A cachet containing 3 gr. of benzo-naphthol and $\frac{1}{4}$ gr. of menthol is useful where there is much flatulence. Izal in 2 min. capsules has been particularly successful in some cases of paratyphoid infections. Thymol, manganese dioxide, hydrogen peroxide and ichthyol have all been recommended by different observers.

Instead of attempting to render the bowel aseptic, Metchnikoff advised the introduction of lactic-acid-producing organisms which are antagonistic to the growth of putrefactive bacteria. Soured milk has long been a staple article of diet among oriental people; it enjoys a high repute as a hygienic measure and is claimed to promote longevity. This lactic-acid treatment has been ridiculously boomed. In many cases no living bacilli or the wrong organisms were taken. In others the cases were totally unsuitable. The treatment is contra-indicated in hyperchlorhydria and rheumatism, and in cases where the intestinal disturbance is due to abnormal fermentation of the carbohydrates. Tablets of all kinds are unsatisfactory as a method of administration of such delicate organisms, and only fluid cultures or milk actually soured by, and containing the bacilli, should be used. This is better than simply giving lactic acid, which is almost certainly absorbed before the point where it is required is reached. Apart from cases where benefit is derived from this treatment, simply by suggestion, or because it enables a patient to take a considerable quantity of a nourishing and usually easily digested food, a specific action can only be expected where the microbe responsible cannot flourish in an acid medium. The reaction of the fæces will be a guide: if they are acid, this treatment is unsuitable, if they are alkaline at first but yield a fair quantity of gas in the fermentation tube, and then show an acid reaction, the treatment will probably not be successful. Good results can only be expected when the fresh fæces are alkaline, and remain alkaline after twenty-four hours yielding hardly any gas to the fermentation tube.

4 *Guelpa's distoxication method* may be given a trial in robust subjects, in view of the excellent results claimed for it by various observers. The method is as follows. For three or four days and sometimes longer, a bottle of purgative water is taken. Guelpa recommends that the following mixture should be dissolved in half a litre of boiling water—

Magnesium citrate ℥ x
Calcined magnesia gr. xxx
Sodium chloride gr. xv
Essence of citron ♏ x

This is to be taken in the morning quite hot, in two doses at ten minutes' interval. During these days no food of any sort is taken, but a mineral water, such as Evian, is drunk freely; or a tisane, such as tilleul, sweetened with a little saccharin. As after all fasting procedures, ordinary diet should only be cautiously resumed.

5. Plombières douches are much advocated by some authorities. The douches should never be given more than three times a day, and never under a pressure of more than 18 inches. Nor should they be continued more than for three weeks at a time, otherwise they are certain to produce colitis.

6. *Vaccine Treatment.*—This has yielded good results in several cases. Elaborate means may have to be taken to identify the responsible microbe. A plate culture is made from the stools and the effect of the patient's blood in agglutinating or destroying the more definitely pathogenic organisms tried. A positive reaction would justify the use of a vaccine prepared from such organisms.

7. *Mechanical Supports.*—Where there is definite visceroptosis much help may be derived by a well-fitting abdominal support, and of these, in my opinion, Curtis's is by far the best.

8. *Surgical Procedures.*—Irrigation of the colon through an appendicostomy wound, short circuiting, and even excision of the colon have all been advised but should only be considered where all medical means have been exhausted without improvement.

W. L. B.

TREATMENT OF DISEASES OF METABOLISM

DIABETES MELLITUS

Corresponding to the age of the patient and the degree of the glycosuria, very different results may be expected in the treatment of diabetes. Generally speaking, the younger the patient, the less amenable will he be. The treatment of ordinary cases is still mainly negative, the aim being to diminish the glycosuria and to prevent the occurrence of acid intoxication, for only exceptionally can we go deeper and attack the origin of the metabolic defect in some definite disease of a ductless gland. With increase in our knowledge of the internal secretions we may look forward to being able to do this more frequently. Naturally, a careful search should be made for evidence of disease of the pancreas, thyreoid or hypophysis, and, if found, appropriate treatment should be applied.

The first step in the treatment of diabetes was Rollo's discovery that limitation of the carbohydrate intake was followed by diminution of the glycosuria and by relief of symptoms. For many years the whole aim was to discover an absolutely carbohydrate-free diet and to restrict the patient rigidly to this. This conception was based on inadequate knowledge and ignored the following facts—

1. Proteins contain fractions which can yield sugar, and excessive protein diet is so stimulating in its metabolic effect that it causes further breakdown of the tissues, with consequent setting free of more carbohydrate molecules.

2. The failure of a diabetic to metabolise carbohydrates is seldom absolute, and careful search will generally reveal some form in which they can be tolerated to at any rate a limited extent.

3. Assimilation of some carbohydrate is essential to metabolism; in its entire absence the body has to draw on fats which it is unable to oxidise completely without their aid. This results in the formation of abnormal fatty acids. To eliminate these the body has to provide ammonia from its protein and calcium from the tissues generally, thus increasing the wasting.

It will be seen that an absolutely carbohydrate-free diet or a total failure to utilise carbohydrate must result in a metabolic disaster in which protein, fats and mineral salts alike share. Coma is the clinical expression of such disaster. The craving of the individual for a mixed diet is the unconscious expression of a fundamental physiological fact.

At best, this search for a carbohydrate-free diet was the outcome of a negative ideal and had but a limited aim. The newer conception offers far greater possibilities of permutations and combinations in the diet to suit the metabolic defect in each individual case. Incidentally, it thrusts the drug treatment of diabetes more than ever into the background.

We may summarise the indications for treatment in diabetes thus—

1. Control of the hyperglycæmia, which involves loss of energy and is the cause of many complications.
2. Increase in the patient's tolerance of carbohydrates.
3. Prevention or control of acidosis.
4. Treatment of complications.

These indications are not independent of each other; thus, increasing sugar tolerance automatically diminishes both hyperglycæmia and acidosis.

Before beginning treatment the amount of sugar in a twenty-four-hour specimen of the urine is estimated on an ordinary diet. Diacetic acid is also tested for by ferric chloride. If this reagent imparts a claret colour to the urine while the patient is still on an ordinary diet, the case is a severe one, and special caution must be exercised in establishing restrictions. A sudden restriction of the diet is unjustifiable and involves grave risk of coma. This risk is, moreover, increased by confining the patient to bed during the process of restriction. At first no starch, but all the sugar except that contained in a pint of milk, is removed from the diet. A mixture of alkalies is prescribed as explained under *Acidosis*. The urine is tested daily for sugar and diacetic acid; so long as the former falls without the appearance of the latter, restrictions may be steadily increased. Thus only a small amount of milk should be allowed in tea or coffee, and bread should be reduced to 2 oz. at two meals a day. The idea that toast is less injurious than bread is fallacious; the only advantage of it is that as it requires more mastication less of it is usually eaten. But being drier it contains a higher percentage of carbohydrate. If the diacetic reaction appears at any stage the diet should not be further restricted for a time, but it need not be relaxed at once unless the reaction becomes distinctly more marked, for diacetic acid makes a temporary appearance in any one on a restricted diet. If the case is going on well, sugar will gradually disappear from the urine at some stage in this process.

The part played by alcoholic excess in

producing glycosuria, usually of an amenable sort, must be remembered. Champagne is particularly apt to excite it in some people. Yet, as shown later, moderate amounts of alcohol may help in severe diabetes.

It is important to determine as accurately as possible the degree of tolerance of carbohydrate in each case. For this purpose some standard diet of known carbohydrate content is necessary. The following is the one suggested by Von Noorden—

Breakfast.—Coffee or tea with one or two tablespoonfuls of thick cream, 6 oz.; hot or cold meat (weighed after cooking), 3 oz.; butter; two eggs with bacon; white bread, 2 oz.

Lunch.—Two eggs (cooked as desired, but without flour); meat, about 6 oz.; vegetables, such as spinach, cabbage, cauliflower, asparagus, prepared with broth, butter or other fat, eggs or cream, but without flour; cheese and butter, 1 oz.; two glasses of light wine; one cup of coffee, with one or two tablespoonfuls of thick cream; white bread, 2 oz.

Dinner.—Clear meat soup (with eggs or vegetables); one or two meat dishes with vegetables, salad of lettuce or tomatoes; wine; no bread.

Drinks.—One or two bottles of ærated waters.

If this diet, which contains about 100 gm. of carbohydrate, does not cause any glycosuria, then the bread is gradually increased until sugar appears. If sugar does appear with this diet, it may be continued for a few days until the sugar is constant and the bread then diminished.

If the urine becomes free from sugar on a restricted diet without diacetic acid making more than a temporary appearance, the restrictions should be maintained for at least a month. Physiological rest allows of at any rate a partial recovery in the sugar-forming apparatus, and as long as abnormal acids do not persist no harm is done to general metabolism. Then a cautious relaxation should be attempted. The following principles must guide us in carrying this out.

Wheat flour is often badly tolerated, and the greatest difficulty is to find a satisfactory substitute for bread. Gluten bread was introduced by Bouchardat in 1841; it is prepared by washing away the starch from flour, leaving the more tenacious vegetable protein behind. It is almost impossible to wash away all the starch, and gluten bread nearly always gives a blue colour with iodine. But it is easy to remove enough starch to leave a very unpalatable residue, and, sooner or later, the patient revolts against it. I seldom use gluten bread as a routine, employing instead limited quantities of ordinary bread if it can be tolerated, or the Brusson-Jeune rolls, which contain less starch than bread and are palatable. Casoid bread or Kalari biscuits taste better than gluten bread, and are free from starch; they should be given a trial. If the patient cannot do with as much starch as is contained in Brusson-Jeune rolls, it is advisable to interpolate days on which gluten, casoid or protene bread is given. Other substitutes for bread are made from aleuronat flour, soya beans or almonds, but, like gluten bread, they are expensive and soon become distasteful. They may be acceptable for a change.

Potatoes are generally tolerated better than bread; in fact, a "potato cure" has been instituted in which they are given largely, but this is not advisable since tolerance for them is limited. On relaxing the diet it is well to add one and then two potatoes of average size (*i. e.* about 3 oz. each in weight) to the daily food, watching the effect upon the urine.

Of all the forms of carbohydrate, oatmeal is usually best tolerated and is strongly recommended by Von Noorden; 8 oz. are given in the day, either as gruel, in cases of impending coma, or as porridge or oatcake with eggs on certain days in the course of treatment. I have been favourably impressed by it, and there is a general agreement as to its value.

Fruit sugar (levulose) can often be assimilated up to 50 gm. (rather less than $1\frac{2}{3}$ oz.) in a day, cautiously given in doses of not more than 5 dr. at a time. If more is given than can be consumed by the tissues at once, it will be stored as glycogen and subsequently turned into dextrose, which will be excreted. Its cost, however, is prohibitive except for wealthy patients or in emergencies such as threatened coma. I have seen striking benefit from its use. Artichokes are rich in inulin, which breaks down into levulose. This provides a cheaper way of supplying levulose, and I have given moderate amounts of artichokes without increasing glycosuria.

Our object, then, should be to select from potatoes, oatmeal or artichokes the form of carbohydrate which can best be assimilated. If the urine cannot be freed from sugar in this way, the next step is to investigate the effects of various proteins on the glycosuria. Meat proteins may have a distinct influence in maintaining it. This, which is insisted upon by Von Noorden, is often overlooked and the patient is allowed to take meat freely. As a matter of fact, he can often take a vegetable diet, which must contain a good deal of carbohydrate, better than he can manage a carbohydrate-free diet with abundant meat. It is not so much that the carbohydrate fraction of the meat protein is not well borne as that the meat has a stimulating effect on the tissue metabolism.

Recent observations of Thompson and Wallace on the increase of glycosuria when meat extracts were given support this view, though I may add that some cases I investigated with Dr. Roper did not show intolerance to meat extracts. However, when we find that either meat or oatmeal can be tolerated separately, but not when given together, we must conclude that meat proteins diminish the tolerance of the body for carbohydrate in many cases.

Von Noorden finds that the order of tolerance is: meat proteins least, then casein, next cooked eggs, and, finally, vegetable proteins, especially in the form of glidine, best of all. The best scheme seems to be to alternate the days of carbohydrate-free diet with days of oatmeal diet and days on which little but eggs and vegetables are taken. Fast days with rest in bed may also be interpolated, as on Guelpa's plan (see p. 168). But in cases with marked acidosis this is not free from risk.

I will give one or two examples of such schemes, but as every diabetic is a law unto himself, careful investigation is necessary to find a plan which suits each case.

1. Vegetable, egg and oatmeal scheme.

In the course of an ordinary restricted diet a week of the following diets is introduced once in six or eight weeks—

(*a*) For two days a diet of lettuce, cabbage, spinach, veal broth, three eggs, butter, two lemons for lemonade and coffee. (Personally, I prefer to do without the veal broth, if possible, for reasons already given.)

(*b*) For three days a diet of 8 oz. of oatmeal as porridge or oatcake, 4 oz. of butter, five eggs, two lemons and coffee.

(*c*) Two days of (*a*) again.

2. Three weeks of restricted diet, *i. e.* no carbohydrate, with the addition of 60 gm. (approximately 2 oz.) of bread. One day of vegetable-egg diet; one fasting day—only weak tea, lemon-squash or whisky-and-soda in suitable cases are allowed, with rest in bed. One day of vegetable-egg diet; four days of carbohydrate-free diet. Then the same scheme begins anew. This plan is one recommended recently, among others, by Von Noorden at the International Medical Congress.

3. Von Noorden records another instance in which a patient kept well for years, exhibiting remarkable energy and remaining free from complications on the following scheme: The ordinary diet was limited in protein and contained 80 gm. (approximately 2½ oz.) of bread daily; every fifth day, a vegetable-egg diet was employed, and, every second month, a series of vegetable-oatmeal days.

4. Marcel Labbé advises the following diet, which may be given for two or three days at a time—300 gm. (about 9 oz.) of leguminous vegetables (peas, broad beans, haricot beans, lentils, soya beans), some green vegetables, 150 gm. (about 4½ oz.) of butter, 5 or 6 eggs, 3 to 6 aleurone heads, and a little red wine.

A marked increase of tolerance of carbohydrate often follows. I have generally used the first and last of these schemes, and have noted a distinct improvement, the urine becoming quite free from sugar in some cases—at any rate for a time. In any case I am accustomed to recommend entire abstention from meat one day in each week. It is necessary, from time to time, to see how the patient tolerates different carbohydrates. If the urine cannot be rendered free by any means, the best point at which to maintain the patient's metabolism is that to which the intake of carbohydrate can be raised without increasing glycosuria while diminishing the acetonuria.

It is clear that some of these schemes can be carried out much better in a nursing home. It is almost impossible to keep records of the intake and output in the patient's own home, and Cammidge has recently emphasised the importance of quantitative as well as qualitative regulation of the intake. After the food has been regularly weighed for some time, the patient quickly learns to judge with the eye the approximate weight of the food he is taking, and then the treatment can be continued at home after his tolerance for different forms of carbohydrate has been estimated.

Control of Acidosis.—Recognition of the significance of acidosis has profoundly modified our treatment of diabetes. It is probable that there are never more than traces of acetone in the urine though it may be present in the breath. Hurtley has recently shown that the nitroprusside test, which was thought to be a test for acetonuria, is really a more sensitive test for diacetic acid. In any case, acetone is a mere decomposition product of diacetic acid which, in its turn, is derived from the breaking down of fats that almost always occurs during starvation or even deprivation of carbohydrate.

It naturally follows that the most effective treatment of acidosis is to find a form of carbohydrate which can be assimilated. Then the fall in the amount of both diacetic acid and sugar in the urine is often striking.

Investigations have been made as to the possibility of replacing carbohydrate in metabolism. Citric and glutaric acids do so to a limited extent. Citrates can be added to the alkaline mixture, which should always be given when the diet is being restricted or when acidosis is marked. Alcohol appears to be able to replace carbohydrate rather more satisfactorily. Bearing in mind the dangers of the alcohol habit and that alcoholic excess excites glycosuria, it is nevertheless advisable

to give alcohol in acidosis to the extent of about an ounce of the pure spirit in the day. Malt liquor, sweet wines, champagnes and liqueurs must be avoided. Since diacetic acid comes from the breaking down of fats, the question arises as to the advisability of giving fat in food. To do without fat would be to deprive the patient of an important source of energy, and it is a relief to find that the administration of fats in the food does not apparently increase acidosis. The only exceptions to this are the lower, more volatile, fats. Butter, therefore, should be kneaded in water before the diabetic eats it, for in this way the more volatile fats are extracted.

The use of alkalies in acidosis is an essential part of the treatment. Spriggs has pointed out that in the normal individual 2 dr. of bicarbonate of soda will render the urine alkaline for twenty-four hours, but if an excess of acids is being formed this is not enough, so that the amount of alkali that can be taken without neutralising the urine is a rough measure of the degree of acidosis.

In some cases it is impossible to render the urine alkaline at all, and I have seen a case where, with the fullest doses of alkali (*i. e.* about 1 oz. every three hours) the acidity of the urine was still twice that of normal. A more accurate measure of acidosis is the amount of ammonia in the urine, which can quickly be estimated by the formalin method. This also has a prognostic value, for a marked rise in the ammonia suggests the risk of coma, though Naunyn's statement that if the ammonia excretion reaches 4 gm. a day nothing can prevent coma is too dogmatic. The normal output of ammonia nitrogen is about 1 gm. a day, and, in severe cases of acidosis, may easily reach 3 gm. If the condition improves under treatment, the urine will become alkaline, and the amount of alkali may gradually become diminished without the return of the acid reaction. It is not sufficient to give sodium alone, as is so often done, for other metallic bases are also being drained from the tissues, particularly calcium. Also, if one metallic salt is given out of proportion to the others, it increases the excretion of those others. I employ the following mixture, based upon the relative proportions of the metals normally present in the urine—

Sod. Bicarb. ʒ i
Pot. Citrat. gr. xxx
Calcii Lactat. gr. iii
Mag. Carb. gr. iii
Aq. ad. ℥ i.

This is given three times a day, and increased up to three-hourly doses, according to the severity of the case.

It has been urged against this method that it increases the intensity of the diacetic reaction in the urine, at any rate for a time. But this is merely because the excretion of the acetone bodies is being facilitated, not because their production is being increased. They are now excreted as metallic diacetates instead of in combination with ammonia derived from the breaking down of the proteins of the tissues. This alkaline treatment should never be omitted in severe diabetes. That it is not more successful shows that we do not yet completely understand the pathology of acidosis. The breakdown of proteins probably plays a larger part in it than is at present realised.

Drug Treatment of Diabetes.—Though alkalies are of distinct value in the treatment of acidosis, drugs have a very limited application to the treatment of glycosuria. Codeia has the greatest reputation in this respect, and apparently helps in some cases. It probably acts by depressing the general metabolism. It is apparently excreted as a glycuronate, and it must be remembered that this substance reduces Fehling's solution. Recently I saw a man who had had glycosuria for some years and who was taking codeia. He still had a small amount of reducing substance in his urine. I did not think it was sugar, and on testing with phenyl hydrazine obtained the osazone of glycuronic acid and not of dextrose, showing that the persistent reducing substance was due to the codeia he was taking. This is a serious source of fallacy which must not be overlooked. In any case, it is quite unnecessary to give codeia when there is merely a trace of sugar in the urine.

Salicylates, also, have some reputation in the treatment of glycosuria. The chief objection to their use is that they mask the ferric chloride reaction for diacetic acid in the urine. They do not mask the nitroprusside reaction, however. As it is probable that salicylates can promote synthesis of purins in the body, there is no inherent improbability that they can help in the synthesis of carbohydrate also, though we have no proof of this. On the whole, I have not been greatly impressed with the action of salicylates in glycosuria. Aspirin has been used, but Von Noorden has observed the onset of nephritis during its administration. It was not certain that the aspirin was responsible, but no other cause could be found.

Arsenic occasionally seems to help, and other drugs such as jambul may diminish glycosuria, at any rate for a time; 5 to 30 gr. of the latter can be given in cachets. Its prolonged use is apt to set up gastric irritation. I have never observed improvement which could be attributed to any other drugs.

After-Treatment.—When the urine has been

rendered free from sugar, lowered tolerance for sugar and hyperglycæmia will probably persist. Before we can pronounce a patient cured we must know that the sugar tolerance has been restored to normal limits, and that there is no excess of sugar in the blood.

In cases of intermittent glycosuria it will generally be found between the attacks that a small quantity of dextrose will produce glycosuria and that there is still an excess of sugar in the blood.

All this indicates the advisability of keeping the patient on the same line of treatment for a considerable time after the urine has become free from sugar.

In this connection, reference should be made to those cases of so-called renal diabetes in which there is no excess of sugar in the blood, but rather a diminution. These cases of hypoglycæmia do not show much response to diet and are probably of a comparatively harmless nature. Garrod, however, has reported a case in a boy whose elder sister had typical diabetes. This hardly suggests that renal glycosuria is entirely distinct from ordinary diabetes, and as a precautionary measure we should in such cases prescribe restriction of carbohydrates in the diet, but not their complete absence.

Spa Treatment.—For a more detailed account of appropriate spas in the treatment of diabetes, reference should be made to the article on *Climatology*. In general, it may be said that it is only the milder cases that are amenable to spa treatment. There is considerable risk in sending a thin diabetic, who is passing a good deal of diacetic acid, on a long journey, and I have certainly seen patients made worse in this way. Carlsbad, Marienbad and Neuenahr are not likely to be visited by English patients for many years. The milder régime carried out at the Hermitage, Evian, may suit some cases, and there are full facilities there for dietetic treatment to be carried out combined with rest in pleasant surroundings.

Treatment of Complications

1. **Diabetic Coma.**—Once coma is thoroughly established nothing more than a temporary rally can be expected, but a good deal can be done in the way of prophylaxis, as has been described in the treatment of acidosis. Carbuncles, overfatigue and constipation are potent factors in provoking coma. On the first suggestion of drowsiness, air-hunger, burning pain in the pharynx or epigastrium, or bilious attacks, the administration of alkalies should be increased and 5 dr. of levulose should be given three times a day. A very extensive relaxation of the diet is probably inadvisable, but 2 pints of milk, though it will increase the glycosuria, may help in impending coma.

If there has been persistent constipation it is a wise measure, which I have found occasionally successful, to have the rectum cleared out and 3 per cent. of bicarbonate of soda with 4 per cent. of levulose given by drop enema until about a litre of fluid has been given.

When coma has developed despite these measures the case is hopeless and a temporary rally is the most that can be hoped for. This, however, may be of great value in order to enable the patient to sign a will and to recognise his friends. About 30 oz. of normal saline, containing 2 per cent. of sodium bicarbonate, may be run slowly into the median basilic vein at about body temperature. It is well to remove from 7 to 15 oz. of blood first. A similar infusion may be given into the other arm four to six hours later. The temporary improvement is sometimes striking. Stronger solutions are sometimes recommended, such as 5 per cent. of sodium carbonate. The addition of sodium acetate, 1 per cent., has been advised, but I have no personal experience of it. Some authorities believe that normal saline is as effective as the alkaline fluid, but I have not found it so. I have added 2 per cent. of levulose to the fluid, but am not convinced that it is advantageous when the patient is actually comatose.

The treatment of other complications of diabetes resolves itself into the diminution of the glycosuria with the application of ordinary principles to the special lesion. Thus—

2. **Diabetic Neuritis**, which is apt to occur in all persistent cases to a greater or less extent, soon clears up when the sugar disappears from the urine. The condition sometimes simulates tabes. Aspirin may relieve the pains very considerably. When they can be borne, massage, ionisation and electrical baths are a great help. The complete ophthalmoplegia which sometimes occurs in diabetes is apparently due to neuritis. The prognosis is not bad. Treatment, in addition to appropriate diet, consists in giving strychnine internally, and electricity. Dr. E. P. Cumberbatch has kindly sent me the following note on this subject: "Electrical treatment may be applied to the orbital muscles when paralysed, but it is difficult to carry out because these muscles lie deeply, and currents that are sufficient to cause them to contract would cause too much pain in the conjunctiva and produce disagreeable sensations by stimulating the retina. Some improvement, however, may follow electrical treatment, and it is not essential that visible contraction of the muscles should be produced. A continuous current should be passed through the orbital cavity, one electrode being a small sponge moistened with 1 per cent. salt solution and placed on the closed lids.

This electrode should be the kathode. The anode may be placed on the neck. The current should be made to vary in strength slowly and rhythmically. The discharges of small capacity condensers may prove to be of value in the treatment of ophthalmoplegia. These discharges are of exceedingly short duration, and, if they are sufficiently brief, may not appreciably excite the sensory nerve or the retina."

Other palsies are rare, but Dr. Edmund Hobhouse has told me of a case of abductor paralysis of the vocal cords with glycosuria which cleared up when the sugar disappeared from the urine.

3. **Perforating ulcer** only occurs when neuritis already exists. Beyond treatment of the neuritis, all pressure must be taken off by complete rest, sodden epithelium removed, the ulcer washed with equal parts of warm water and 10 vol. per cent. of hydrogen peroxide two or three times a day, and then well dusted with equal parts of zinc oxide and starch powder. It may be advisable to use, as a preliminary measure, boroglyceride fomentations, thoroughly wrung out, or a bath containing a little liquor iodi or permanganate of potash.

4. **Gangrene** if truly diabetic in nature only occurs, like the perforating ulcer, when there is neuritis. But an elderly diabetic seems unusually prone to atheromatous gangrene. In the former condition the knee-jerks will have gone, the gangrene is moist, and diacetic acid is almost certain to be present in the urine; in the latter the knee-jerks may be present, the gangrene is much drier, and there need be no acidosis. The treatment will vary according to which of these two conditions are present. In the former every effort must be made to diminish the hyperglycæmia, which provides the micro-organisms with abundant pabulum. The local treatment may be carried out on the same lines as for perforating ulcer. Early amputation is indicated, as the gangrene tends to spread rapidly. The defective sensibility of the legs in neuritis necessitates caution in the use of hot-water bottles, which may produce gangrene by causing sores. If arteriosclerosis is the cause of the gangrene, vaso-dilators and diffusible stimulants should be given, and the part warmly wrapped up. Here, too, operation will probably become necessary, but there is not the same need for haste, as the gangrene does not tend to spread in the same way and a definite line of demarcation will appear. The small ulcerated patches over the internal malleoli are not really perforating ulcers or allied to gangrene. They may appear while the knee-jerks are still present. They originate in the sebaceous glands. They should be treated by cutting a piece of lint to the shape of the patch, moistening it with a stimulating lotion such as 2 gr. of zinc sulphate to an ounce of water, and renewing it every day. The lint is then covered with a piece of oiled silk, also cut to the size of the patch, and bandaged. After three days of this treatment a dusting powder of zinc oxide and starch should be used instead.

5. **Carbuncle.**—This is a serious complication in diabetes, both on its own account and because it may excite coma. If it is small a ring of collodion may be painted round it to produce hyperæmia and prevent its spread. The use of a suction cup after a small incision has been warmly recommended. The suction should always stop short of producing pain. Short repeated applications are better than a single prolonged one. Three to six applications, lasting five minutes each, with intervals of three minutes between, are advised by J. M. Graham. Ionisation may be tried with a zinc needle as the positive pole inserted into the middle of the swelling. An old-fashioned remedy is the injection of a drop of pure carbolic acid into the carbuncle. If it does not yield quickly it will probably be necessary to make a free incision into it and scrape out the slough. Dressings with sterile horse serum have been found useful. In chronic cases an appropriate vaccine should be tried. It is of the first importance to support the patient's general condition, which is liable to become profoundly asthenic.

6. **Pruritus** of the vulva is a common complication, and may be the first thing to call attention to the glycosuria. It generally subsides quickly if the glycosuria can be controlled. Of local measures the best is frequent bathing with subsequent application of a lotion composed of glycerine of tannic acid and sulphurous acid, ½ to 1 dr. of each in an ounce of distilled water. This prevents fermentative changes in the saccharine urine which sets up the pruritus. An ointment of 10 gr. of menthol in an ounce of vaseline, or a lotion of 20 min. of chloroform in an ounce of olive oil may help to allay the itching. Pruritus of the glans penis is much less common, and should be treated on similar lines.

7. **Eczema** should be treated on ordinary lines.

8. **Respiratory complications,** such as phthisis, bronchopneumonia and gangrene of the lung, must be treated in the usual way. Phthisis generally runs a rapid bronchopneumonic course. The patient must not be too strictly dieted, and the sugar may disappear spontaneously from the urine as the tuberculosis advances.

9. **Albuminuria.**—The association of albuminuria with glycosuria is common. In some of these the glycosuria is "renal" in nature, that is to say, it is accompanied by hypoglycæmia. In this case treatment should be

concentrated on the kidney condition, as the glycosuria has not much significance. In others alcoholic excess may be responsible, and if this is corrected the glycosuria soon proves amenable. In one such case I saw, even moderate restriction of the amount of alcohol caused the glycosuria to clear up, only to return with each drinking bout. On the other hand, prolonged glycosuria almost inevitably leads to albuminuria in time, probably from irritation of the kidney. As long as it does not cause raised tension, cardiac hypertrophy and other signs of cardio-vascular disease, one need not trouble very much about the albuminuria. The treatment is merely that of the glycosuria.

10. **Digestive disturbances** are fortunately rare. They may arise from excessive intake of proteins, for which the best thing is a few days of Von Noorden's vegetable, egg and oatmeal diets, or even twenty-four hours practical abstention from food. When digestive symptoms are severe and accompanied by paroxysms of pain it is probable that the glycosuria depends on a definite pancreatic lesion which calls for treatment. (See *Diseases of the Pancreas*.)

11. **Ocular Complications.**— Ophthalmoplegia due to neuritis has already been considered. For the treatment of cataract, the most frequent of the ocular complications, reference must be made to works on ophthalmic surgery. Retinitis may occur in simple diabetes, but is more likely to be met with when there is a kidney lesion as well. The treatment is that of the cause. Diabetic amblyopia due to a central scotoma is in my experience only met with in smokers. As the amount of tobacco consumed has sometimes been quite small, I conclude that the symptom is due to the action of combined toxins. Entire abstention from tobacco seems to be necessary in such cases. When tobacco amblyopia occurs in a moderate smoker suspect glycosuria.

12. **Diabetic Collapse.**—In some cases the patient may be suddenly attacked with alarming collapse. The extremities and the face become livid and the pulse becomes small and very frequent. The patient becomes drowsy and will probably die within a few hours, but there is no evidence of acetonuria. R. T. Williamson has called attention to the importance of this condition, which is generally attributed to myocardial degeneration, and should be treated on the same lines as acute heart failure from any other cause. The intravenous injection of a pint of saline containing $\frac{1}{250}$ gr. of strophanthin and oxygen inhalations are probably the best methods to adopt.

13. **Mental Complications.**—Most diabetics are irritable and many are unduly suspicious. Occasionally these symptoms may be intensified into delusions with suicidal or homicidal impulses, or the patient may become melancholic. Such cases should be treated on the ordinary lines of a toxic insanity. The treatment of the glycosuria must be persisted in.

14. **Pregnancy.**—Diabetes generally causes amenorrhœa and conception is rare. If it occurs the fœtus dies *in utero* in about two-thirds of the cases, often with hydramnios. The interests of the mother are therefore paramount when they conflict with those of the child. Pregnancy may be allowed to go to full term as long as the mother's condition improves under treatment and the bulk of the uterus is not excessive. But if the glycosuria remains at a high level, if there is hydramnios, or if other unsatisfactory symptoms occur the pregnancy should be terminated, especially if former pregnancies ended by the birth of a dead child. Naturally it must be clear that the glycosuria preceded the pregnancy, and that it is not merely the glycosuria or lactosuria of pregnancy. Even though pregnancy is well borne, the diabetes will probably get worse afterwards; it is therefore best avoided.

W. L. B.

DIABETES INSIPIDUS

Different causes may produce polyuria of the kind to which the name of Diabetes Insipidus has been applied. The recognition of this fact is essential to the proper treatment of what is really a symptom. A persistent polyuria without the presence of albumin or sugar may result from (1) syphilitic meningitis, especially of the base of the brain; (2) disease of the hypophysis cerebri; (3) a primary defect of the kidney which renders it incapable of secreting concentrated urine; (4) polydipsia.

1. The frequency with which syphilitic meningitis is responsible for diabetes insipidus makes it imperative that in every case Wassermann's reaction should be tried before treatment is undertaken. I have obtained a strongly positive reaction in a boy with diabetes insipidus who certainly presented no other stigmata of congenital syphilis. Meningitis affecting the interpeduncular space would be likely to irritate the hypophysis cerebri, so that this type is sometimes similar in its origin to the one to be described next, but is usually more amenable to treatment. Daily inunction of a drachm of mercurial ointment and administration of potassium iodide must be carried out. At the present time, the feeling is in favour of giving rather full doses of potassium iodide, *e. g.* 8 to 15 gr. or more three times a day for a fortnight at a time, with intervals of a fortnight without any.

As to the advisability of neosalvarsan in

conditions depending on cerebral and congenital syphilis, see the article on syphilis.

2. The cases of hypophyseal origin are the worst and most progressive because they usually depend upon a new growth. The head should be skiagraphed in all cases, great care being taken to get the rays exactly transverse to the clinoid processes. The best plan appears to be to place a bullet in each external acoustic meatus and to adjust the position of the head, and the direction of the rays, until the shadows of the bullets are accurately superposed. The cases which become drowsy and then comatose, with ocular disturbances, such as bi-temporal hemianopsia and optic atrophy, or where glycosuria ensues in the later stages, will almost certainly prove to be of hypophyseal origin. Cushing's experimental observations on this subject are of great importance. The pharmacological action of pituitrin is to raise the general blood pressure by vaso-constriction while dilating the renal vessels, thus causing diuresis. According to Schäfer, the effect of a second injection is more diuretic without general vaso-constriction, so that the effect of repeated injections is analogous to the condition seen in diabetes insipidus. Such cases are not likely to respond to treatment. If there is evidence of a progressive tumour of the hypophysis cerebri, operation would have to be considered as offering the only and that not a good chance in a grave disease.

As the condition is presumably due to over-secretion, there does not appear to be any use in giving extracts of the gland or of its adjuvant, the thyreoid. The internal secretion of the pancreas is opposed to that of the hypophysis as regards glycosuria, but I am not aware that pancreatic extract has proved of any benefit, though it might reasonably be given a trial in hypophyseal diabetes insipidus. Treatment must be mainly symptomatic, as described below. The sinister significance usually attached to diabetes insipidus is probably due to these hypophyseal cases, for the other forms of the disease are consistent with life and health for many years. It is quite probable that the temporary polyuria following head injuries is set up by irritation of the hypophysis cerebri, and the fact that over-secretion of this gland can be evoked by nervous stimuli may explain hysterical polyuria.

3. In the form associated with the primary defect in the kidneys, the patient is incapable of secreting urine of a normal concentration, so that he requires a much greater quantity of water to remove the normal products of metabolism. According to Meyer, the condition may be recognised by the reaction to the administration of 20 grm. (5 dr.) of sodium chloride, which will be excreted very slowly here, but not in the other types where the kidney, being sound, can respond by excreting it within twenty-four hours. In this renal type of the disease, the excretion of the ingested salt may take a considerable time, even some days. It will be noted that there is a resemblance between this condition and an interstitial nephritis in which the power of secreting concentrated urine and salt is also distinctly reduced, while the minute trace of albumen is hardly detected in such a large amount of fluid. Indeed, in some *post-mortem* records of diabetes insipidus, it is by no means clear that the condition of the kidney was really distinct from chronic interstitial nephritis. Observations of the blood pressure are badly needed; if this proves to be definitely raised, it provides an additional point of resemblance with interstitial nephritis. Meyer has introduced another interesting test for recognising this condition. Theocin-sodium-acetate increases the permeability of the kidney, and where this permeability is reduced for solids, the drug, by facilitating their excretion, does away with the necessity for further dilution of the urine. Therefore, though it ordinarily acts as a diuretic, here it merely raises the concentration of the urine without increasing the amount of fluid. Applying this test in the case of syphilitic origin, I found that theocin-sodium-acetate raised the excretion of water from 5,600 to 8000 c.c. It should be noted that the doses formerly recommended are now considered excessive, and that 2 gr. twice a day will probably be found sufficient. It follows that restriction of the ingested fluids is a futile and cruel procedure. The patient *must* excrete a dilute fluid, and, if fluid is not given to him, he must obtain it from his own tissues. He loses weight, and the output of nitrogen rises, showing that the deprivation of water is producing tissue breakdown. This increased excretion of nitrogen in turn demands more excretion of water. The appetite and the general health will soon suffer, while the distress from thirst becomes extreme.

But I am not yet satisfied that this type is entirely distinct from the hypophyseal form. In the syndrome of infantilism with interstitial nephritis and recrudescent rickets described by Morley Fletcher, the hypophysis cerebri may be enlarged and the condition approximates to this renal type of diabetes insipidus. Moreover, Saundby has pointed out that in diabetes insipidus the cause of death may be the gradual destruction of kidney substance producing uræmia.

Treatment should be directed towards diminishing the solids that have to be excreted by the kidneys, this being an important factor in producing the polyuria. To this end, the amount of salts should be rigidly restricted

and all meat extracts forbidden. The amount of protein should be reduced. The patient can be encouraged to make up with carbohydrates and fats, which will diminish his appetite for nitrogenous food, and meat should certainly not be allowed more than once a day, and then only in small quantities. Tea, coffee and alcohol should also be avoided.

4. If the Wassermann reaction is negative, if the skiagram of the skull is normal, and if 20 grm. of sodium chloride do not provoke well-marked diuresis while theocin-sodium-acetate does, the probability is that polyuria is secondary to the excess of fluid imbibed. Ralfe advised that if the fluid ingested and excreted approximately balanced, the amount of fluid drunk should be reduced by 2 pints; if this is followed by a fall in the urine excreted, the fluid drunk is reduced by another pint every third day, but, as soon as there is no more reduction in diuresis, the intake should not be restricted any further. It should be noted that this method was originally suggested for diabetes insipidus in general, but from the foregoing considerations it will be clear that it is only likely to meet with success in cases secondary to polydipsia.

Symptomatic Treatment.—While the origin of many cases remains obscure, much of our treatment must remain symptomatic. Acidulated drinks, or $\frac{1}{2}$ oz. of raw oatmeal stirred into 2 pints of water and flavoured with lemon are pleasant. During any period of restriction of fluid the patient may temporarily alleviate thirst by frequently rinsing the mouth out with water without swallowing it. I have found the sucking of acid drops to increase the thirst. A small dose, $\frac{1}{20}$ gr., of pilocarpin may relieve the dryness of the mouth. Whatever the origin of the case, tea, coffee, alcohol and salt are inadvisable.

The drug which has the greatest reputation in the symptomatic treatment is valerian. As much as $\frac{1}{2}$ oz. of the tincture has been given four times a day, with apparently good results. It may be reinforced with advantage by 5–10 min. of tincture of cannabis indica, and some bromide of ammonium. Valerianate of zinc has also been advocated in large doses, such as 15 gr. gradually increasing to 30, three times a day. I have never used it in such large amounts, but with 8 gr. in the day I have noted that while the output falls, the intake rises, and I suspect that the drug acts largely by causing retention of water in the tissues. Ergot (10 min. of the fluid extract three times daily) may cause temporary benefit, but a careful look-out must be kept for symptoms of ergotism. Arsenic and iron are useful adjuvants as tonics. Electrical treatment has been recommended by Robertson in the form of the constant current, with the positive pole at the back of the head, and the negative passed along the floor of the nose until the cervical spine is reached. Starting with a current of $\frac{1}{2}$ ma., this is gradually increased to 5 ma. The duration of the application is at first one minute, increased every second or third day until it is used for five or six minutes. A seven weeks' course is advised.

But before treatment can be put on a really satisfactory basis more complete observations will have to be made in each case to determine the origin of the symptoms. At the present time, the theory of a direct or indirect overaction of the hypophysis cerebri seems to offer the best clue. W. L. B.

GOUT

The treatment of gout at the present time reflects the changing views as to its pathology. Formerly gout was regarded as simply due to retention of the uric acid derived from the food which became deposited as insoluble biurate of soda in those peripheral structures where circulation was sluggish and the proportion of sodium high. The inflammatory changes in the joints were regarded merely as the result of mechanical irritation by the biurate crystals, while the cardio-vascular changes were attributed to uric acid increasing the viscosity of the blood, thereby impeding the circulation. On this view, the rational treatment was considered to be abstention from the purin bodies in the food which produce uric acid and administration of drugs credited with being uric acid solvents. Three main facts have led to a modification in this point of view: (1) mere excess of uric acid will not cause gout, for in leukæmia the amount of uric acid formed is about ten times the normal, yet gout does not follow. (2) In the normal animal the liver can destroy uric acid rapidly, so that even if the kidneys are prevented from excreting properly no retention of uric acid occurs. Therefore, in gout we have to postulate a failure in the uricolytic ferments of the liver. This may possibly be the result of an intestinal intoxication. (3) However strictly the intake may be limited, the body can still produce uric acid in considerable quantities. The endogenous formation of purins plays a larger part in the pathology of gout than was formerly suspected. As Sir James Goodhart says: "Though you exclude absolutely all uric-acid-forming food . . . you may wither up your patient into a shrivelled, juiceless, prematurely aged being, and there will yet, under favourable conditions, be squeezed out of his tissues enough uric acid to form a large deposit of red crystalline matter in his urine." There is apparently an inability to katabolise purins whether from the food or in the tissues,

probably due to hepatic insufficiency, just as in cystinuria or alkaptonuria. But unlike these, the insufficiency does not show itself from birth, although there is undoubted hereditary transmission.

"Gout has tended to become prevalent among peoples who, after periods of stress and struggle, have attained to conditions of material well-being, who have aggregated into cities which become the centres of increasing luxury and more elaborate civilisation" (Garrod). Thus it was common in Imperial Rome. The history of the individual repeats that of the race, and gout is apt to occur in those who, after a strenuous earlier life with plenty of exercise, settle down to a sedentary and comfortable middle age with abundance of good living. There is a general agreement that gout is becoming less frequent at the present time, even allowing for the fact that many diseases formerly labelled gouty are no longer considered so. Greater moderation in eating and especially in drinking the heavier forms of alcohol, a more open-air life with rational physical exercise are probably the principal factors in this decrease.

The treatment of the gouty paroxysm is still frankly empirical, while an attempt is made to place the treatment of the gouty state on a rational basis. For that reason we will deal with the latter first, though it must be admitted that many of the means adopted still lack rational sanction.

1. Treatment of the Gouty State

The gouty subject should be encouraged to take up some form of out-door exercise and sufficient occupations or hobbies to prevent the morbid introspection to which he is prone. Worry is a fertile cause of attacks in some, and I have known heads of families who were carefully screened from anxieties by the other members in self-defence, for if they were not so sheltered they could always revenge themselves by an attack of gout. Heavy dinners and late hours should be forbidden. Careful attention will, of course, be paid to the state of the bowels. For this purpose the Compound Colocynth pill or a pill containing 2 gr. of iridin, 1 gr. of euonymin and extract of hyoscyamus q.s. may be given. A routine use of an aperient water may be indicated every morning.

Dietetic Treatment.—Here the purin-containing foods claim our consideration first. Purins contain the group C_5N_4, and uric acid is merely one of the more abundant and more highly oxidised of them. The urinary purins are derived from (1) the food, either as (*a*) free purins, xanthin and hypoxanthin in meat juices, (*b*) bound purins from the nucleoproteins of the cell nuclei, and (*c*) methyl-purins in tea, coffee and cocoa, (2) endogenous purins formed within the body chiefly by the muscles and leucocytes. It follows that the more cells the food contains the more purin will it yield. The accompanying table from Walker Hall's analyses will show the relative amounts of purins in ordinary articles of diet.

	Purins in Grains per pound.
Fish :	
Cod	4·07
Salmon	8·15
Meat :	
Mutton	6·75
Beef	7·96–14·45
Chicken	9·06
Liver	19·26
Sweetbread	70·43
Eggs and cheese	almost 0
Vegetables :	
White bread, rice, cabbage, cauliflower, lettuce	0
Potatoes	0·14
Asparagus	1·5
Peas	2·54
Oatmeal	3·46
Beans	4·16
Beverages :	Purins in Grains per pint.
Wines	0
Milk	0·0014
Beer	1·09–1·27
	Methyl-purins Grains per teacup.
Tea, China	0·75
Tea, Ceylon	1·21
Coffee	1·7

From this it will be noted that milk, eggs, cheese, white bread, butter, rice and most vegetables except the pulses are practically free from purins. On the other hand, it will be seen that the usual distinction drawn between red and white meat is entirely fallacious if it is intended, as it presumably is, to refer to the amount of purins contained, for chicken contains more than mutton, while sweetbread is extremely rich in them. Luff maintains, nevertheless, that sweetbread is harmless, since its nuclein portion is only slightly absorbed. But it is certain that the administration of sweetbread to a healthy man is followed by a greatly increased excretion of uric acid, while this is much less pronounced in the case of a gouty subject. As Garrod well says: "If the knowledge which we possess does not justify us in pronouncing sweetbread to be

undesirable food for gouty people, we must admit that we are not yet in a position to give any advice on this subject on scientific, as distinguished from empirical, lines." Other internal organs, such as liver and kidney, are inadvisable on similar grounds.

Strong animal soups and meat extracts are definitely contra-indicated, as they contain purin bodies without a corresponding amount of nourishment.

It is usual to forbid gouty patients asparagus, presumably on account of the small quantity of purin which it contains, but considering that this only amounts to 1·5 gr. in a pound of asparagus, it is really negligible and, in my opinion, the diuretic effect of asparagus renders it quite a suitable vegetable for the gouty. Peas, oatmeal and beans do contain a definite amount of purin, and the last two had better be taken to a limited extent only.

In general terms leaves are better than roots so far as vegetables are concerned. Spinach may be allowed except when oxaluria is present. Fresh fruit such as pears, green figs, oranges and grapes may be allowed. The sweeter, richer fruits such as dates, are less suitable. Lemons may be allowed, for the citric acid which they contain will become bicarbonate in the blood and, therefore, does not cause acidity. Preserves are usually better avoided on account of the fermentation which has usually taken place. In spite of Linnæus's advocacy of strawberries, Garrod advises gouty patients to avoid them. There is no special reason to avoid sugar, as is usually done, unless there is a tendency to obesity. Fats have no real influence in gout except (1) as a factor in obesity; (2) as rendering food less digestible. Thus, when things are cooked in fat, they are likely to cause dyspepsia by inhibiting the secretion of gastric juice.

Beverages.—There can be little doubt that alcohol plays an important part in the production of gout, especially in the form of malt liquors, port and liqueurs. Sherry is injurious to some and champagne to others, although they do not contain purin bodies as beer does. The lighter white wines, such as still hock or moselle, may be taken when the patient is unwilling to do without alcohol either because he is accustomed to it or because he finds it a stimulant to digestion. Well-diluted whisky in moderation may be allowed for these reasons, but there is little doubt that every gouty person is decidedly better without alcohol at all. Tea and coffee are often forbidden on the ground that they contain methyl purins, but as they are excreted without being converted into uric acid, it seems a mistake to deprive the patient of these valuable stimulants. If they do not disagree with the digestion, they are not likely to increase the gouty symptoms. Cocoa, on the other hand, is too rich and fattening to be a suitable beverage, quite apart from its purin content. Hard water is frequently condemned though without any very clear reason. It is hardly necessary to point out that the "chalk stones" do not contain any calcium salts at all, and, therefore, there is no reason why a chalky water should increase them. Apart from its constipating effect, there is nothing in hard water to do a gouty patient harm. Mineral waters of all kinds have been freely used in the treatment of gout. In fact, the chemical constitution of various waters advised has been so widely different as to suggest that the active ingredient in them all has been the water. As Osler says: "Much of the humbuggery of the profession still lingers about mineral waters, more particularly about the so-called lithia waters." Still, not to take too sceptical an attitude of this subject, we may inquire into the most suitable springs for the purpose.

Spa and Bath Treatment. — The principal benefits appear to have been derived from (1) radio-active water, such as that of Bath or Buxton, (2) alkaline waters such as those of Vichy or Royat, and (3) sulphur-containing waters such as those of Harrogate, Llandrindod, Strathpeffer, or Aix-les-Bains, which presumably act by remedying the intestinal condition. But, in every case, a large share in the benefit must be ascribed to the regulated life and freedom from worry which is an essential part of spa treatment. Most spas are now fitted up with all sorts of mechanical and electrical aids to treatment, which, while they do not indicate any excessive faith in the efficacy of the springs on the part of the management, are a valuable aid to treatment. The various balneological measures which may be used in chronic arthritis are fully described in the article on *Chronic Diseases of the Joints* (q.v.). For further details of suitable spas the reader should consult the article on *Balneology and Climatology*.

Warm baths may be a help if the skin has ulcerated over the chalk stones, by dissolving some of the exposed biurate of soda. Thus, a 2 per cent. solution of potassium carbonate may be used quite warm in an arm bath, though not for long enough to make the surrounding tissues sodden. In addition to the other measures described under chronic diseases of the joints, ionisation may be a decided assistance. For this purpose lithium salts may be used on the positive pole and 2 per cent. salicylates or tincture of iodine on the negative. A much stronger current can be used with salicylate than with iodine. Another method is to employ 1 to 2·5 per cent. solution of sodium chloride on the negative pole, a current

of 5 milliamperes per square centimetre of surface being passed for twenty minutes. Such applications may be used once a fortnight.

Uric Acid Solvents. — Few drugs have any real action as solvents of uric acid in the tissues; our altered views on the significance of uric acid in gout also diminishes our ardour in trying to effect this.

Lithium salts held for long a high reputation for this purpose simply because lithium urate is much more soluble than the potassium or sodium salt. On chemical grounds it is impossible for this claim to be substantiated. Chemical action is determined both by the mass and avidity of the various interacting bodies and also by the law that in any mixture of acid and bases it is the insoluble combination that occurs. The few grains of lithia which can be introduced into the body cannot possibly contend with all the sodium present there, which, in addition to having the advantages of mass reaction, forms the less soluble salt. Moreover, if enough lithium could be introduced for this purpose, it would be definitely poisonous. The only value of lithia water is in the water itself.

Piperazin had a vogue some years ago until it was shown that in the quantities which could be taken it had no solvent action in the body although it had in the test-tube. This is explained by the fact that when several salts are added to uric acid in a test-tube the solvent action of piperazin is much reduced. We may conclude that the salts in the blood act in the same way.

Lycetol and lysidin, which are closely allied to piperazin, have failed for similar reasons.

Urotropin was advocated on the grounds that the formaldehyde it gives rise to forms a soluble urate. In the body, however, it does not increase the uric acid output to any real extent.

Salicylic Acid and its derivatives, on the other hand, definitely increase and may double the uric acid output in the normal individual on a purin-free diet. It may even have this effect after five years of a purin-free diet. This can scarcely be due to washing out of retained uric acid, for, in view of its rapid destruction normally by the liver, such retention can hardly occur. As there is not a marked loss of weight when salicylates are given, the doubled output cannot be due to doubled breakdown of the tissues. By a process of exclusion we are forced to the view that it actually causes a synthetic production of purins, though there is no direct evidence of this. It would certainly be curious if, in our anxiety to wash out uric acid, we were really increasing its endogenous production.

Thyminic Acid (solurol) was recommended by Minkowski in the belief that uric acid is normally carried in solution combined with this organic acid. The number of recorded successes with the drug remains very small, however, and its use appears to be making but little headway.

Atophan (phenylchinolin-carbonic acid) is the most recent addition to the uric acid solvents. That it will, in some cases, increase the uric acid output to an extraordinary degree is certain. When taken by a healthy individual the excretion of uric acid, even on a purin-free diet, rises at once, and then slowly falls, returning to normal by the third or fourth day. When uric acid is injected into a normal man its excretion is spread over several days, and the total amount injected is not recovered; but if the injection is given during a course of atophan the whole of the uric acid is completely excreted within twenty-four hours. According to Walker Hall, the same results are obtained in a gouty individual, so that, under the influence of this drug, the gouty and the healthy renal cell appear to excrete just the same amount of uric acid. Its administration appears to shorten the acute stage of gout, and is accompanied by increased uric acid output. So far as it goes this might be held to support the retention theory; more probably, however, both retention and constitutional disturbances are due to the same unknown perversion of metabolism, and the drug affects the endogenous formation of purins. Atophan is put up in tablets containing seven and a half gr., four to six of which should be given in a day broken up in plenty of water. Weintraud, who warmly recommends it, advises full doses of sodium bicarbonate at the same time, such as half an ounce on the first day and a drachm and a half on subsequent days. The method is well worth a trial, both in acute and chronic gout. In the latter I have had considerable success by giving atophan for one week in each month. It is obviously contra-indicated in urinary calculus and gravel. In view of the insolubility of the sodium salts and their abundance in the body, it would appear more rational to give some at least of the alkali in the form of potassium salts, and this I have done. For a similar reason Sir W. Roberts advised patients to restrict their use of table salt, substituting potassium chloride as far as possible. Perhaps we might go further and check the addition of table salt to the food altogether.

The *alkaline treatment* of gout has little experimental evidence in its support. In severe diabetes there is often a definite diminution in the alkalinity of the blood, but this is not the type of glycosuria in which gouty symptoms occur. Sir William Roberts, although he said of himself that "few practi-

tioners had employed alkaline remedies in gout with more determination," finally decided against their utility.

Other drugs which have had considerable vogue in the treatment of chronic gout are potassium iodide and guaiacum. They may be given a trial, but it would seem that many of the successes recorded were in cases which were more probably rheumatoid arthritis.

2. Treatment of the Gouty Paroxysm

Besides the general treatment suitable to a febrile state, the affected joints should be raised and protected. Application of cold to or leeching of the joints is to be avoided. A hot lotion containing an ounce each of bicarbonate of soda, glycerine and tincture of opium in 12 ounces of water will afford much relief, though, in deference to the pharmacologists who deny the local effects of opium, this might be omitted. Internally, nothing is so effective as *colchicum;* we do not understand its action, though, as it causes a temporary diminution in the number of leucocytes, it may lessen the production of endogenous uric acid. The subsequent return of the leucocytes would account for the failure of the drug to exert a prolonged influence. Ten minims of the Vinum Colchici or the Tr. Colchici Semin. should be given every four hours for a few days. It is usually combined with 10 gr. of *carbonate of magnesia* or *salicylate of soda*. The latter drug cannot be justified rationally in view of its apparent action in increasing the endogenous uric acid, though empirically it seems to relieve pain. Caution must be exercised with colchicum, as it causes purging or faintness in some patients. If it cannot be borne, *atophan* may be substituted, and, in any case, it is worth while to give this drug when the colchicum is stopped.

Citarin, a compound of formaldehyde and citric acid, has been recommended in doses of 15–30 gr. three times a day. It is incompatible with alkalis. *Potassium citrate* is often useful as a diuretic which also renders the urine less acid. If none of the above drugs suit the case, a mixture of *iodide and bromide of potassium* may be tried. If the kidneys are sound, 10–15 gr. of *Dover's powder* may be given at night. It is well to avoid all meat, meat juices and alcohol during the acute stage.

3. Treatment of Suppressed and Irregular Gout

Almost every condition characteristic of the middle and degenerative periods of life have been thus described, but the evidence that they are really gouty in nature is often quite unsatisfactory. Suppressed or retrocedent gout is a name applied to alarming and often fatal symptoms referable to the alimentary canal (pain, vomiting and diarrhœa), the cardiovascular system (dyspnœa, palpitations, syncopal and anginal attacks), and the nervous system (headache, twitchings, delirium and coma). They are said to come on as a result of a chilling of or the direct application of cold to affected joints, and they certainly may be accompanied by a diminution of the local signs. It can hardly be doubted, however, that they are essentially uræmic in character and should be treated as such. The following manifestations are usually regarded as irregular gout—

1. *Cutaneous System.*—Eczema. On this point Adamson says that "one may see hundreds of cases of eczema without meeting with a case of gout; in fact, a gouty patient is practically unknown in a skin clinic." Clearly, then, the treatment should be that of eczema (*q.v.*). Dupuytren's contraction of the palmar fascia has no proved affinities with gout.

2. *Special Senses.*—Episcleritis and conjunctivitis (the "hot itching eye" of gout), iritis and glaucoma, have all been referred to a gouty origin. For their treatment reference must be made to a work on ophthalmic surgery.

3. *Nervous System.*—Migraine, neuralgia, neuritis and sciatica have been attributed to gout with varying degrees of probability. The treatment is that of chronic gout in addition to that of the local conditions (*q.v.*).

4. *Respiratory System.*—We may observe that true spasmodic asthma is more likely to occur in gouty families rather than in patients with gout. Any one who has chronic bronchitis long enough will become emphysematous, when a secondary asthma is liable to follow. From implication of the heart or kidneys, so-called cardiac or uræmic asthma may result, which is, of course, an entirely different thing. In each of these cases the treatment is that of the local conditions rather than of gout.

5. *Circulatory System.*—Gout may set up interstitial nephritis and atheroma with their attendant effects on the cardio-vascular system. For the prophylactic and early treatment of such conditions see the article on *Chronic Interstitial Nephritis*. Recurrent phlebitis, especially in the legs, is often attributed to gout. It is quite as often due, in all probability, to infections and intoxications from various sources, especially the alimentary tract (see article on *Intestinal Intoxications*).

6. *Digestive System.*—"Bilious attacks" are common, in which the tongue is furred, the breath offensive and the bowels constipated: the liver is said to be sluggish, but certainly some of these attacks are due to B. coli infections, as are the "gouty" cystitis and urethritis.

7. For "*gouty*" *glycosuria* see the article on *Diabetes*.

W. L. B.

OBESITY

The term obesity includes four distinct clinical types, namely: ordinary obesity, anæmic obesity, toxic obesity, and internal secretory obesity. Treatment will inevitably depend upon a recognition of the predisposing cause. *Ordinary obesity*, or, as it is sometimes inelegantly termed, "the middle-aged spread," may be regarded as the outcome of a lack of balance between the physiological intake and output; in other words, the patient is one who eats too well or works too little, or both. *Anæmic obesity* is frequently seen in chlorosis and after profuse hæmorrhage from whatever cause; it depends upon an insufficiency of hæmoglobin and consequently of oxygen, whereby the metabolism of fats is reduced. *Toxic obesity* is due to the presence either of substances which reduce metabolism, such as alcohol, mercury, arsenic, or of poisons such as that of typhoid fever, whose action it is to exhaust the metabolic activities. *Internal secretory obesity* is the outcome of a disturbance of the balance which subsists between the various internal secretory glands. Transient forms of such obesity are sometimes seen at puberty, and are induced by factors such as marriage, maternity, lactation. But the class includes forms, such as the obesity of the menopause, adiposis dolorosa (Dercum's disease), myxœdema, and lipomatosis universalis asexualis, which are persistent in their nature although they may be induced to yield to appropriate treatment.

Ordinary Obesity.—Drugs play but a small part in the treatment of ordinary obesity; it is largely a matter of exercise and diet. Various systems of diet are in vogue, and of these Banting's and Salisbury's are undoubtedly the best. By these methods the fats and carbohydrates are reduced, the nitrogenous elements are very much increased, and large quantities of water are consumed. Although frequently attended by considerable success, it must be borne in mind that these measures place an enormous strain upon the kidneys, and that the ingestion of nitrogenous substances in large quantities tends to the production of high blood pressure and consequent arteriosclerosis. Before resorting to such vigorous treatment the physician should in all cases assure himself that the condition of the patient in these directions leaves nothing to be desired. Where this assurance is lacking, treatment must be confined to limiting the general intake, especially of fats and alcohol, at the same time increasing the output by suitable means, notably massage, Turkish baths, special exercises, and exercise in the open air. Undoubtedly the best method of managing these patients is by a course of treatment at a spa, such as Vichy or Marienbad.

Exercises.—With the approach of middle life, though there may be no tendency on the part of the individual to eat more, there is almost certainly an inclination to do less. For this reason advancing age is in many instances accompanied by an increasing fleshiness, the deposition of fat being usually most marked in the region of the abdomen. The chief agent in effecting oxidation is admittedly muscular exercise, and it is a fact, though one which is not sufficiently recognised, that fat is very readily deposited in the neighbourhood of relaxed and atrophied muscles. Now it is just the muscles of the anterior abdominal wall for which the usual forms of exercise, such as walking and golf, undertaken by the man of middle age, provide little or no exertion. As a consequence, these muscles become atrophied and flaccid, and the figure acquires the dreaded aldermanic curve. It is necessary that a determined effort should be made to restore to these muscles something of their original tone. Exercise in the open air, although recommended upon general principles, is useless as a means of reducing local adiposity; this will yield only to local exercises, of which the following will be found to be very efficacious. They should be performed immediately upon rising, with the window open and wearing as little clothing as possible. The patient lies flat on his back upon the floor with a weight upon his feet to prevent their rising from the floor. The feet should be thrust under the opened bottom drawer of the chest of drawers. With his arms folded on his chest the patient pulls himself into a sitting posture by means of his abdominal muscles, taking care not to bend the knees. This should be done three or four times, increasing the number with practice until the manœuvre can be performed seven or eight times in succession without undue fatigue. When this can be accomplished the patient should attempt to perform the same exercise, but with this difference, that the arms are extended above the head in a line with the body. Care must be taken that the arms do not advance beyond the line of the trunk. This exercise is more difficult than the first; it should, however, be persevered with until it can be performed eight to ten times in succession. Next, releasing his feet and still lying upon his back, with arms crossed upon his chest, the patient should endeavour to raise both legs from the floor without bending the knees, until they form a line at right angles to the trunk. Other exercises which may be attempted are: (*a*) To touch the toes without bending the knees; (*b*) Extended on the floor with head and heels touching the ground and arms crossed upon the chest, to raise the trunk from the ground in the manner of an arch by means of the trunk muscles alone. These

exercises should be performed slowly and deliberately, and as proficiency is attained the number of times they are performed in succession should be increased. Their continued and regular practice is followed by a reduction of "front" and a reappearance of the waistline to a degree which is sometimes positively astonishing.

Massage and Zander and Swedish exercises are to be recommended, but they must be employed with discretion. Much harm has been done, resulting in cases of hernia and other abdominal complaints, by the employment of over-drastic methods.

Turkish baths and electric-light baths promote metabolism and are therefore valuable adjuncts to other treatment. There is no class of patient which responds more readily to spa treatment than the ordinarily obese. Not only are the general principles of the treatment, such as diet, massage, exercise and baths, more easily applied and more efficiently enforced than at home, but the patient receives a mental stimulus from the regular life and changed surroundings which plays no small part in effecting a cure. The obese tend to be indolent in mind as they are lethargic in body. Mental activity is a great promoter of oxidation, and for this reason a factor which ensures distraction and employment of mind has a therapeutic value which it is difficult to over-estimate. It must be borne in mind, however, that the success of spa treatment depends in the first instance upon the right choice of a spa. Marienbad, Carlsbad, Homburg, Kissingen, Vichy, Vittel, Evian, Aix-les-Bains, Brides-les-Bains are all indicated.

Drugs play but a minor part in the therapeutics of obesity, and in the large majority of cases they are unnecessary. Their rôle is confined to promoting metabolism and to assisting the functions of the excretory organs. In no case should a direct action upon the adipose tissue be aimed at, and drugs such as iodide of potassium and thyreoid extract should be left severely alone. The marked effect of thyreoid extract in reducing adiposity is only too well known; its harmful influence in other directions is, unfortunately, less well recognised.

Although in its graver forms it is more likely to produce emaciation, a very common cause of obesity is chronic constipation. A good method of managing these cases is by a course of sulphate of magnesia, 5 gr. of blue pill being given once a week. But the use of paraffin oil, which is now so general, if it be really persevered with, is certainly the best means of overcoming constipation. Dyspeptics may be treated with soda and bismuth, and all obese patients will derive benefit from a diuretic, such as ½ oz. of infusion of buchu given in half a tumbler of Evian water half an hour before each meal.

Diet.—Whatever attitude the physician may adopt in regard to the diet of an obese patient, there are two directions in which no latitude is permissible. The intake of common salt must be severely limited, and no fluids should be allowed with meals. During the first fortnight salt should be eliminated altogether from the dietary; later on it may be used sparingly, but the amount should never exceed 160 gr. a day. By this measure a double object is achieved. In the first place, the amount of HCl in the gastric secretion is reduced and appetite is in consequence less keen; moreover, food without salt being unpalatable, the patient is never tempted to eat to excess. In the second place, the ingestion of salt favours that accumulation and stagnation of fluid in the lymph spaces which is so prejudicial to efficient metabolism. Fluids may be taken half an hour before or an hour after meals, never with them. The point is one which needs emphasis, and neglect to supply a patient with precise directions may lead to disappointment in the results of an otherwise rational treatment.

The Vegetarian System is a favourite one in France, and it has this very distinct advantage: it may be employed without prejudice in cases where the more drastic regimes, such as Banting's and Salisbury's, are excluded by reason of the state of the patient's arteries and kidneys. The diet is almost exclusively composed of green vegetables, such as cabbage, cauliflower, spinach, etc., reinforced by eggs, milk and cheese. It has the merit of providing food in a quantity sufficient to stay the patient's appetite, but of a quality so low in nutritive powers that weight is rapidly lost. The drawback to the system lies in the fact that unless the food values are carefully controlled, the nitrogenous intake is liable to be inadequate. Moreover, many patients have so great a distaste for a vegetarian dietary that to enforce it is to impose upon them a hardship.

Banting's, Salisbury's and Ebstein's systems are fully described in the textbooks of dietetics (*Textbook of Diet and Dietetics*, edited by G. A. Sutherland). The following is a dietary of moderate severity which should produce a reduction of about 1 lb. per week.

Dietary. 8 *a.m.*—A tumbler of hot water, sipped, to which some fresh lemon-juice may be added.

Breakfast. 8.15 *a.m.*—One small cup of tea or coffee sweetened with saxin or saccharin; no cream, no milk; 1 oz. dry toast; no butter; 4 to 6 oz. of lean grilled steak, chop or kidney, lean cold tongue, chicken, game, grilled or boiled sole, plaice, cod, turbot, brill, haddock or whiting.

1 *p.m.*—Three-quarters of a tumbler of Evian, Vittel or Vichy water.

Lunch: 1.30 *p.m.*—3 to 4 oz. of lean beef, mutton, lamb, chicken, game, hot or cold, roast or boiled; gravy must be free from fat; 4 oz. of any vegetable as given below plainly boiled without butter, lard or oil; a baked apple, or 2 to 3 oz. of baked cherries or gooseberries, sweetened with saxin or saccharine only; salad, if taken, must be without oil or beetroot; two to three Wine Oliver biscuits; 2 oz. of toast; one glass of light wine, red or white; small cup of coffee, without sugar, milk or cream, but sweetened with saxin or saccharin.

5 *to* 6 *p.m.*—A cup or two of tea without milk or sugar and one Wine Oliver biscuit; half an hour before dinner three-quarters of a tumbler of any of the above-mentioned waters.

Dinner.—3 to 4 oz. of any fish, as at breakfast, and 4 oz. of any meat, as at lunch; if chicken or game is taken it must be without bread sauce or crumbs; if less fish is taken the meat may be increased proportionately; 4 to 6 oz. of any vegetable as mentioned below, and 3 to 4 oz. of baked or stewed apples, rhubarb, cherries, or gooseberries, sweetened with saxin or saccharin only; salad and biscuit as at lunch; 2 oz. of toast; wine as at lunch; a cup of black coffee with saxin or saccharin.

A cup of beef-tea may be taken at bedtime, but a tumblerful of any of the above-mentioned waters is preferable.

Condiments Allowed.—Worcester and anchovy sauces; ketchup, pepper, mustard, vinegar, walnut pickle, horse-radish; not more than 160 gr. of salt may be taken per diem.

Salads and Vegetables Allowed.—Watercress, radishes, lettuce, cucumber, mustard and cress, spinach, asparagus, celery, brussels sprouts, cabbage of all kinds, cauliflower, broccoli, sea or Scotch kale, vegetable marrow, kidney or French beans, tomatoes, artichokes, endive, sorrel, salsify.

Anything not mentioned above may be assumed to be forbidden.

It is not the writer's intention to enter here into the details of the treatment of *Anæmic Obesity* or of *Toxic Obesity*. A recognition of the underlying cause points inevitably to the course which should be adopted.

Internal Secretory Obesity.—That a disturbance of the balance which subsists between the functions of the internal secretory glands is a cause of well-marked metabolic derangement has long been known. Much has been written upon the subject, more especially by physicians of the French school, but in the present imperfect state of our knowledge it is difficult to lay down definite lines for the pursuance of treatment. It is important that the physician should possess a clear view of the manner in which these glands act and react upon one another, for such knowledge alone will provide him with the key to the treatment of obesity arising from internal secretory derangement.

It is well known to breeders of animals that suppression of the activities of the sexual glands leads to an increased deposition of fat; hence the custom of castrating animals which are to be fattened for market. This rule holds good in the case of man and is applicable to individuals of both sexes. The pathological obesity of children, cases such as are seen in abundance at spas of the Salines-Moutiers class, is invariably associated with deficient development of the genital organs. Examination will show that obese boys possess testicles of the infantile type. That cessation of sexual activity leads to increased adiposity in the female is shown by the results of double ovariotomy, while the obesity of the menopause is a condition with which every one is familiar. Insufficiency, which is short of complete absence, either of the thyreoid or the hypophyseal secretion frequently results in the deposit of mucin in the tissues in quantities so large that a condition resembling general obesity is produced. Such conditions are lipomatosis universalis asexualis, now more generally known as Fröhlich's syndrome, and adiposis dolorosa (Dercum's disease). *Fröhlich's syndrome* is believed to be the outcome of hypophyseal insufficiency. It is common to both sexes and may make its appearance before or after puberty. It is characterised by pseudo-obesity of very pronounced type; where the onset is before puberty, by skeletal undergrowth; and by complete sexual impotence, the genitals either remaining infantile or reverting to the infantile type. The prognosis is bad and a rational method of treatment has not as yet been evolved. Pituitary extract (anterior lobe) has, however, done good in some cases, and should be tried. *Adiposis dolorosa* is a disease of middle life confined almost exclusively to women and appearing at or after the menopause. Its origin is obscure, but it is believed to be the outcome of some type of thyreoid inadequacy, and it has been associated with hypophyseal tumour. There are four stigmata of the disease, namely: adiposity, spontaneous pains with tenderness, muscular weakness, and psychic manifestations. The onset is gradual. There is frequently extreme general obesity with irregular fatty tumours; nodular raised areas appear which are soft, painful and tender; these never affect the face, hands or feet. Pain is spontaneous, and may be elicited by pressure; it is probably due to interstitial neuritis of the nerves of the adipose tissue. Prognosis is good as to life, but bad as to recovery. Treatment is almost entirely confined to relief of the symptoms. Thyreoid extract should always be tried, and hypophyseal has been known to afford a measure of relief.

So little is at present known of the manner in which the ductless glands react upon one another that it is difficult to say with certainty which of them plays the leading part in the production of obesity. For this reason it is the height of unwisdom to administer extracts of the glands with the sole object of reducing adiposity. Thyreoid extract should never be given unless, in addition to obesity, the patient shows signs of thyreoid inadequacy. Where a glandular therapy is deemed expedient there are two points which should be kept well in mind; one, that the amount of thyreoid usually given is many times too large; the other, that the amount of hypophyseal extract is usually much too small. The initial dose of thyreoid for a patient suffering from obesity should never exceed ½ gr. of the dried extract twice daily, and even then a careful watch should be kept for signs of intolerance. Hypophyseal extract given by the mouth in doses of 8 to 10 gr. per diem will be found to have a pronounced effect in stimulating the unstriped muscular tissue and favouring general metabolism. Although the extract, when given by subcutaneous injection, raises the blood pressure very notably, this effect appears to be lacking when the drug is given by the mouth.

Prof. Bergonié, of Paris, advocates a system of general electrical muscular exercise with a view of promoting metabolism, and thus of reducing obesity. The system requires a special apparatus which is now installed in various institutions in the large cities and in most of the spas. The results appear to be satisfactory in a fair number of cases. L. W.

RICKETS

Rickets is a disease of general nutrition affecting infants, and, to a less extent, older children, and producing characteristic changes in the bones. In considering its treatment the actual symptoms and signs of the active period of the disease, which is usually short, must be clearly differentiated from the resulting deformities which may persist throughout life. In judging whether a child has rickets in an active stage or whether the disease is quiet, it is necessary to look not only for the presence of the general symptoms, but also for those changes in the bones which are characteristic of the active period of the disease.

Amongst the general symptoms which indicate that the disease is still progressing the most important are abundant sweating of the head, muscular weakness, restlessness and constipation. The characteristic bone changes are those which occur at the epiphyseal ends of the long bones and at the costo-chondral junctions, the latter of course being the growing epiphyseal ends of the ribs. These changes give rise to the enlargement of the epiphyseal regions and to the beading of the ribs which constitute so characteristic a feature of rickets, and which should be accepted as evidence that the disease is still progressing.

This external enlargement of the epiphyseal regions persists, however, for some time after the actual pathological changes have ceased. A more accurate determination of the condition of the epiphyseal cartilages may be made by examining a skiagram. The latter, in active rickets, shows the widening of the cartilage in both directions, and a cup-shaped end to the diaphysis. These appearances alter very rapidly when the active disease ceases, the cartilage interval shrinking to its normal extent and the end of the diaphysis becoming straight and transverse.

Judged by the criterion of a skiagraph, rickets may be said to arise in the second six months of life, and to persist commonly in the active stage until the age of eighteen months to two years. During the third year active rickets is still frequently found, but after this it becomes rapidly less common. Very rarely it persists beyond the age of five, occasionally, however, continuing to the age of eight, nine or even older. Such a condition is properly called "Continued Rickets."

Occasionally the child appears well for a time, and then, owing to alteration in the surroundings or diet, the disease reappears, the characteristic epiphyseal changes returning. This condition may be called "Recrudescent Rickets." Very rarely older children at ages of from ten or twelve to sixteen or eighteen years, are found with rickets which is typical in all respects, the general lassitude and restlessness, muscular weakness and sweating being present, and the epiphyseal changes characteristic. Such cases are properly called "Adolescent Rickets." It is, however, very difficult, if not impossible, to prove that the disease in them is not a recrudescence of an earlier attack.

The period of activity of rickets must then be regarded as variable, and the criterion of its cure should be taken to be the disappearance of the characteristic bone changes. As a rule it is sufficient to judge of these by clinical observations, but in cases in which the enlargement of the epiphyseal regions persists after three or four months of careful treatment, it is advisable to confirm the opinion founded on clinical grounds by means of a skiagraph. The changes occurring at the epiphyseal lines are of course not the only alterations in the bones in active rickets. The subperiosteal and the endosteal growth of bone are also defective. so that the bones are softened throughout, but these changes are not easily demonstrable in

skiagraphs. After recovery such bones as are curved often become thickened and buttressed on the side of the concavity. This buttressing may sometimes yield evidence that the disease has been arrested.

Treatment may be divided into Preventive and Curative, and the latter further considered under general hygiene, diet, drug treatment and the treatment of deformities.

The Prevention of Rickets must depend on the adoption of a proper diet for infants. The disease never manifests itself during the first six or seven months of life in children who are breast-fed, and it is rare in children who have been suckled for twelve or even fifteen months. Breast-feeding must, therefore, be included as one of the important means of prevention. After weaning the one causative factor that is certain is the absence of a sufficiency of fat and protein and the presence of an excess of carbohydrates in the food. Severe rickets is far more common in cities where the mothers work, wean their children early, and substitute starchy foods for milk. The use of condensed milks, which are deficient in soluble protein and usually in fat, and which contain much additional sugar, is a further important causative factor.

But errors of feeding are not the sole cause. The general surroundings of the child are important, rickets being more common and more severe in slum districts where the children are poorly, and often improperly, clad, and where the supply of light and air is defective. Occasionally the whole of a family suffer from severe rickets, the younger children being, as a rule, the more affected, and it is often difficult in such cases to see how the food and surroundings differ from those of neighbouring families in which the children have escaped or have suffered from a mild attack. In fact, there is sometimes a family tendency to suffer from the disease, which cannot at present be explained.

Very occasionally in cases of continued rickets the disease persists for years, even when the child is amongst the very best hygienic surroundings, and is most carefully fed. In such cases some additional visceral disease may be present, and should be looked for. In such children a defect of the kidneys is sometimes present, giving rise to a "Renal Type" of Infantilism which is associated with rickety changes at the epiphyseal lines and with bone deformities. This condition is liable to be mistaken for ordinary uncomplicated rickets; the distinction is important, for, if operative treatment be undertaken for the deformities, the renal insufficiency may lead to a fatal result.

Diet.—The principles of arranging a diet for a child suffering from rickets have already been mentioned; they consist in the addition to the food of extra protein and fat, and the subtraction of carbohydrate particularly in the form of unaltered starch. Further, the feeds or meals must be kept regular in time, and biscuits, cakes and sweets, between meals must be forbidden. The chief food should be fresh cows'-milk, which should not be sterilised or boiled. As children are generally over a year old when they come under treatment, milk-puddings, fresh meat, eggs and fish may be added, and such fat as that of bacon. In older children green vegetables should also be ordered. Potatoes, biscuits, cakes, buns, sweets and condensed milk, should be forbidden, also patent foods, except those known not to contain an excess of starch. Bread should be given in moderate quantities, best in the form of toast and stale crust.

Drugs are of comparatively little value, cod-liver oil and malt, and iron in the form of phosphates are useful, especially amongst the poorer patients, who may find it difficult to get a really adequate supply of proper foods. These drugs should be looked upon as additions to the diet, furnishing certain elements which might otherwise be insufficient.

A child with rickets in whom the diet is corrected and the surroundings not excessively bad, should be cured of the active disease in three months, that is to say, skiagraphs at that time should no longer show the characteristics of activity. A little later, after four or five months at the latest, the external enlargement of the epiphyses and the beading of the ribs should disappear. If the child is not cured as rapidly as this, the home and surroundings must be carefully investigated, and, if necessary, the child should be sent away out of the town, or away from its home for two months. If the disease still continues, a very careful investigation of the patient must be made, in particular any septic focus, such as decayed teeth, must be removed, chronic gastro-intestinal disturbance looked for, and the amount and constitution of the urine investigated. As already stated, very occasionally the active process will persist in spite of every form of treatment. Provided, however, there is no reason to suspect renal disease, it may be confidently predicted that eventually the disease will undergo a spontaneous cure.

Prevention and Treatment of Deformities in Rickets.—Although the bones in rickets are soft, they do not bend unless they are subjected to some more or less continual pressure. Every rickety deformity has, in fact, a mechanical, in addition to the pathological, cause. In considering the prevention and treatment of these deformities it is essential in every case

to inquire into their mechanical cause, and to attempt to counteract it. It must also be remembered that in the majority of cases the bones will be well consolidated after three or four months' treatment, and that the deformities are not likely to progress seriously during that time.

The common alterations in the shape of the chest, Harrison's sulcus and the keeled sternum, are due to some inspiratory obstruction acting in conjunction with the rickety processes. The only method of preventing their increase consists in the removal of any obstruction such as that due to adenoids, and the treatment of the chronic bronchitis that is so common in rickety children.

The spinal deformities, although uncommon, are important, for if any considerable kyphosis or scoliosis has once arisen, the weight of the upper part of the trunk in the standing or sitting position will tend to its increase, even after the active rickety process has ceased. They should, therefore, invariably be treated by the application of a support fitted to the corrected position of the spine, worn night and day, and only removed half an hour daily for exercise and massage. This support must only be omitted when the spine remains quite straight when it is removed.

In the upper limb curvatures of the humerus and of the radius are occasionally produced by crawling. They practically never arise whilst the child is under treatment, so that nothing can be done to prevent them. Nor do they call for corrective treatment.

The most frequent deformities of the lower limbs, bowing outwards and forwards of the femur and tibia, arise before the child has learned to walk; they are due to the cross-legged sitting posture, and not to standing. The erect position may tend to increase them so long as the bones are soft, but such increase as will occur in the course of three months is slight, and it is now very generally agreed that it is better not to apply splints to prevent walking. The loss of the natural muscular action and the pressure of the bandages is likely to affect the nutrition of the limbs, and in the opinion of many, the harm thus done more than counterbalances the benefit derived.

Knock-knee differs in that the mechanical factor in its production is the weight of the body in the erect position, that the deformity may tend to increase after the active disease has ceased, and that the strain thrown upon the knee-joints tends to stretch the ligaments and produce lateral mobility of the joint. Although again it is not advisable to prevent the use of the limbs altogether, some support is necessary, particularly in older children. This should take the form of an outside splint or steel brace fitted below into the boot, the knee being drawn outwards by a knee-cap. The child is thus enabled to walk with a stiff knee.

Treated by such expectant measures with the addition of external support in case of the spine and of knock-knee, rickety deformities in young children tend to improve. Surgical treatment for the purpose of correction is usually unnecessary. Operation should not be advised before the age of four years unless the deformity is of exceptional severity, after the age of four it is well to correct the deformities unless they are slight or are improving rapidly. Curvatures of the tibia are best corrected by osteoclasis, a greenstick fracture being produced which unites rapidly and gives an æsthetic result which is more perfect than that yielded by osteotomy. Genu Valgum in its slighter degrees can be corrected by means of a rack splint in the course of four to six weeks, an outside brace being applied for a few months afterwards. If more severe in degree, Genu Valgum calls for an osteotomy of the femur (McEwen). Other deformities such as bowing of the femur, only very occasionally require correction by operation.

Continued, recrudescent and adolescent rickets, require the same methods of treatment as does the disease when it occurs in infancy. The diet must be modified to suit the age of the child, but the principle of increasing the proportion of fat and proteins, and diminishing the carbohydrates is the same. As already mentioned, some cases of continued rickets are extremely difficult to cure by dieting and hygienic measures, and in them the evidences of active disease may persist for years. In such cases the deformities tend to progress, and the application of braces is more often necessary. Occasionally in these cases the question will arise as to the expediency of operation for the correction of deformity whilst the disease is still active. In general it may be said that operative treatment is better postponed, but the correction of the deformities by rack splints or braces may be carried out. Very occasionally, when a deformity such as knock-knee is so severe in degree as to prevent walking, it may, however, be desirable to operate in spite of the fact that the disease is active in order that the limb may be brought into use, and a certain amount of exercise taken. R. C. E.

SCURVY, INCLUDING INFANTILE SCURVY

In spite of the divergent views which are held concerning the causation of scurvy, there is a consensus of opinion as to the methods by which it may be prevented and cured.

In 1795 Sir Gilbert Blane obtained the

introduction of lime juice into the British Navy, a measure which was promptly followed by a decrease in the incidence and severity of the disease, quickly converting it from the most terrible scourge to a condition of little moment. The success which has attended anti-scorbutic treatment may be gauged by the following figures: For the twelve years following 1851, 1058 cases were admitted to the Dreadnought Hospital Ship lying off Greenwich. Between 1899 and 1909 ten cases only were reported by Dr. Herbert Williams of the Port of London Sanitary Committee.

The treatment of scurvy is based on the knowledge that there is in fresh vegetables, fruits and animal fluids such as milk and blood, something which is absent in the same substances when dried, and which is capable of preventing scurvy. What this "anti-scorbutic element" actually is, has not been determined. It is present in greatest abundance in fresh green vegetables such as cabbage, lettuce and cress, and in yams, onions and potatoes; fresh fruits, such as limes, oranges, lemons and apples, are rich in it; preserved vegetables and fruits contain it to a less degree. It has been supposed that the organic acids present in certain vegetables and fruits constitute the anti-scorbutic element, but citric and tartaric acids, if administered alone, are of little or no value; the former is not permitted on British ships. Moreover, these acids are not present in some well-recognised anti-scorbutic foods, such as the potato. Sir Alfred Garrod held the view that potassium was deficient in the diet of those who developed scurvy, but there is no constant proportion between the value of a food as an anti-scorbutic and its potassium content. Sir Almroth Wright regards scurvy as an acid-intoxication induced by an absence or deficiency of alkaline foodstuffs, or an excess of acid-containing foods. He divides foods for this purpose into those which, on incineration, leave behind an acid ash, such as meats and cereals; those leaving a neutral ash; and those leaving an alkaline ash, such as roots, tubers, fruits and fruit juices, the blood of animals and milk. It is well known that a diet consisting exclusively of the first group induces scurvy, which may be cured by the administration of the members of the last. Against this view is the fact that scurvy does not resemble closely the condition which may be caused in animals by poisoning with acids. The work of Hölst and Fröhlich makes such a view untenable. These workers have shown that rabbits fed on a scurvy-producing diet (cereals) can only be kept free from scurvy if *fresh* vegetable food is given, and not if the vegetable is dried previously, even if large quantities of sodium bicarbonate be added to it. There is little to support the view that tainted meat is chiefly responsible for scurvy, for it has occurred in children who are breast-fed or fed on sterilised milk; moreover, the signs of ptomaine poisoning are wanting. The opinion that it is infective in origin has little influence on treatment. A rapid transmission of the disease from one community to another has been reported by Dr. Myers Coplans, but it has been contended with reason that the condition which he described was not scurvy but an epidemic form of stomatitis.

Recent work promises to lead to a more scientific and accurate knowledge of the hitherto intangible "anti-scorbutic element." Thus Funk has isolated from various living structures substances to which he has given the name "vitamines." He considers it essential that these should be present in the food if proper growth and development are to be maintained. It is important in connection with the subject of scurvy that he has demonstrated the presence of vitamines in fresh milk, and in many of the anti-scorbutic foods, and more especially that he has isolated them in appreciable amounts from lime juice. According to this observer, vitamines are soluble in water, dialysable, and destroyed by heating to 130° C. They are isolated in a crystalline form and are neither salts nor proteins. Schaumann states that such substances are probably very numerous and at present mostly unknown. They probably seldom exist in the free state, but are constituents of more complicated molecules such as nucleins and phosphatids. Among the diseases which their absence in food produces are scurvy and infantile scurvy. F. Gowland Hopkins in order to study these substances has conducted feeding experiments on a large scale in rats. He has shown that on an artificial diet containing pure proteins, fats, carbohydrates and salts in correct proportions, young rats ceased to grow in about fifteen days, though the addition of a minute quantity of certain tissue extracts and fractions of such extracts secured normal growth. He thinks that little can be said at present as to their chemical nature, but is of opinion that as growth is arrested when these bodies are absent from the dietary, it is reasonable to suppose that diseases of nutrition, such as scurvy, may be produced in like manner.

From what has been said it is clear that prophylactic measures are of the first importance. Ships should carry a supply of preserved vegetables and fruits, and some anti-scorbutic preparation such as lime juice. In this respect short voyages are attended with less risk from scurvy than long ones. Even under the modern improved methods of preservation, fresh vegetables and fruits are more anti-scorbutic than

those which are preserved, so every opportunity should be taken of procuring fresh vegetables when the vessel touches port. Too absolute a reliance should not be placed upon lime juice, for if taken regularly it is apt to become distasteful and may set up digestive or intestinal disorders. For this reason it is difficult to be sure that it is being taken except under conditions of discipline, as in the Royal Navy. The same difficulty to a greater extent underlies the suggestion of Sir Almroth Wright, who recommends the administration of such essential anti-scorbutics as sodium lactate, calcium chloride or Rochelle salt instead of lime juice.

Contributing factors which make for freedom from scurvy are the maintenance of good general health, warm clothing, efficient ventilation and moderate exercise. Good nutritious food, including fresh or well-preserved meat, may be counted among the preventive measures, apart from any specific anti-scorbutic element which they contain.

When the disease is actually present, it yields readily to treatment if the proper remedies are procurable, and in two or three weeks all but the severest cases will end successfully. Generally a diet including green vegetables and fresh fruits is all that is necessary, care being taken that these are not pushed to excess, so that they do not disturb digestion, produce diarrhœa or renew a former dysentery. Lime juice, orange juice or lemon juice are only needed if fresh vegetables or fruits cannot be obtained. Effusions into the pleural or peritoneal cavities may require aspiration if they are bulky or persistent. Absorption of the extravasations under the periosteum may be accelerated by gentle massage if they prove obstinate. In severe cases local treatment may be necessary for the gums, to stop the oozing and assist their hardening and shrinking. An antiseptic and deodorant mouth-wash such as sanitas or Condy's fluid, aided by the application of solid caustic potash or sulphate of copper, fulfils these requirements. If hæmorrhagic ulcers are present they may be bathed with mild antiseptic lotions or normal saline, and should be dressed aseptically in the usual way. During convalescence iron preparations are indicated to treat the anæmia, which is often profound.

Infantile Scurvy

The treatment of scurvy in infants is based on the same principles as in adults. The anti-scorbutic element, however, has to be supplied in diet of a fluid or semi-solid nature. The first essential point is to stop the particular diet which has led to the production of the disease. This is usually some form of proprietary food, especially one which is dessicated or prepared from cereals. Dr. Edmund Cautley gives the diet in 553 collected cases: Proprietary foods 250, sterilised milk 122, pasteurised milk 40, boiled milk 14, humanised milk 6, uncooked cows' milk 5, condensed milk 72, dried milk foods and water only 21, breast milk and additional food 2, breast milk alone 21. As he remarks, "obviously the diet most likely to cause the disease is the one farthest removed in character from human milk, and from fresh, as opposed to cooked, food." If it be considered advisable to feed an infant on a proprietary food or a milk which has been sterilised or subjected to laboratory manipulation, chemical or physical, about a teaspoonful of fresh fruit juice should be given two or three times weekly to minimise the risk of producing scurvy. In all but exceptional cases such forms of food are better avoided.

The scurvy-producing food having been replaced by good fresh milk, the condition will gradually improve in the majority of cases until recovery is complete. The duration of the disease will be shortened by giving fresh fruit juices such as those of oranges, lemons, apples and grapes, sweetened. Potato cream, as recommended by the late Dr. Cheadle, is a valuable remedy. It is made thus: the potato is baked in its skin, the floury part under the skin is scraped off and mixed with milk, in the proportion of a teaspoonful of the potato to an ounce of milk. One to two teaspoonfuls may be given three or four times a day. It is not suitable for infants under seven months old. Raw meat juice, although not a very powerful anti-scorbutic, is useful because it also combats the anæmia. Vegetable soups and purées may be given to children of ten months old and upwards. If the milk is digested with difficulty it may be citrated by adding citrate of soda in the proportion of 2 gr. to the ounce of milk. Sodium lactate or bicarbonate may be used to counteract the diminution of the alkalinity of the blood, which Sir Almroth Wright has shown to be present. In this way it probably lessens the tendency to hæmorrhage.

Very careful nursing is required in cases of infantile scurvy, for the limbs are often so tender that the baby cries out in alarm as one approaches the cot. The weight of the bedclothes should be taken off by means of a cradle, and the tender limbs should be kept at rest by sand bags. If orbital hæmorrhage produces proptosis, the conjunctival sac should be kept bathed with 4 per cent. solution of boracic acid. The gums may be swabbed gently with a mixture of equal parts of lemon and glycerine, or equal parts of glycerinum boracis and glycerinum potassii chloratis. Occasionally the periosteal hæmorrhages are very slow to disappear when the disease is

otherwise over. At this stage, tenderness being no longer present, very gentle massage may be employed to promote their absorption. The anæmia may be treated by raw meat juice, as mentioned above, or by the administration of iron. F. S. L.

TREATMENT OF DISEASES OF THE RESPIRATORY SYSTEM

VACCINE TREATMENT OF DISEASES OF THE UPPER AIR-PASSAGES

It is not within the scope of this article to give an account of work done elsewhere on vaccine treatment of diseases of the upper air-passages. The following description is the result of my personal experience of vaccines made for my patients by Dr. M. H. Gordon of St. Bartholomew's Hospital, during the last seven years.

Great care has been observed in the selection of the patients, and no treatment has been undertaken without repeated examinations. The methods employed consist of—

1. **The Collection of Secretion.**—When taking a specimen from the nose, the vestibule must be carefully cleansed to prevent contamination by superficial organisms. The secretion is then obtained by a platinum loop, forceps, or a swab of sterilised wool wrapped round a probe. In the case of an accessory sinus the nose is first syringed with normal saline solution, and a weak cocaine and adrenalin mixture is applied to the opening of the suspected sinus, so that the discharge shall escape more easily. If this fails, the secretion is aspirated through a canula, or an exploring needle is inserted into the sinus and the discharge expelled into a sterilised bowl by the injection of air or normal saline solution. For rough examinations it is sufficient if the patient blows his nose into sterile gauze. Whenever possible the secretion should be examined at once. Where this is impossible it should be placed in a closed bottle or tube containing sterilised saline solution, to prevent it from drying. Secretion is obtained from the naso-pharynx by suitable forceps or swabs, the tongue being depressed by a spatula, so that the mouth organisms are excluded. An excellent instrument has been devised by C. E. West for this purpose. It consists of a silver tube with a curved end through which runs a wire carrying a swab; the whole appliance can be easily sterilised. When passed into the naso-pharynx or larynx, the swab is pushed out and withdrawn again within the tube before removal of the instrument. Post-nasal secretion or sputum may be obtained by spitting, if the mouth is first cleansed by repeated gargling with sterile water.

2. **Examination of Secretions.** (a) *By Films.*—These are stained by ordinary methods, especially Gram-fuchsin, to determine what organisms are present and to gain a rough idea of their nature and relative number. Such examinations are most important to show whether proper care has been taken in collecting the secretion, whether the organisms persist in the same number at different stages of treatment, and whether there is evidence of phagocytosis.

(b) *By Cultures.*—Whenever possible the collected secretion is smeared at once on blood-agar tubes or plates and incubated at a temperature of 37° C. for twenty-four hours or longer, the various organisms requiring different periods for their growth. The culture must be examined at the end of this interval to determine the principal organisms. The fact that some of these grow more readily than others is important. The prevalent infection must be determined by the number and not by the size of the colonies which have grown, and by comparing the cultures with films made from the secretion. Pure cultures are very rare, but in many instances one type of organism is prevalent, especially influenza or streptococcus. These two are the commonest persistent infections of the nose. The culture more generally found is a mixed one, and in most cases only two organisms are prevalent. In many instances the same combination persists for long periods to the exclusion of everything else. This is found even with relapsing infections such as colds. To make certain of the exact nature of an infection the examinations must be repeated, and, in order that mistakes may be avoided, vaccine treatment should never be begun until this has been done.

Mixed cultures with more than two organisms prevalent are also common in infections of the lower air-passages.

Sterile cultures are almost unknown, with the exception of chronic influenza infections; these are extremely difficult to cultivate, and likely, therefore, to be overlooked.

Contaminations from the mouth, vestibule, skin and air are difficult to avoid, and it is essential that the clinician should consult with his bacteriologist regarding the symptoms of every case. Our observations on these lines have convinced us that it is often possible to say beforehand what the infection is likely to be.

Blood cultures and serum diagnosis may be of great value especially in acute infections. The Opsonic Index is not often of practical value.

3. **Vaccines, Non-sensitised.** (In most of my cases autogenous vaccines have been used in preference to stock preparations.)—The bacteria may be killed by heat or by the action of some chemical agent such as concentrated galactose, ether or phenol. Another method consists in incubating the suspension of bacteria in saline solution or distilled water at 37° C., the result being that after a short time the organisms are killed and undergo autolysis. The vaccine may be put up in sealed glass capsules, each containing a known number of organisms suspended in normal saline solution (1 per cent.) and phenol (0·5 per cent.).

4. **Dosage.**—There is evidence to show that after an injection of vaccine there is a definite period during which the quantity of anti-bodies circulating in the blood is decreased. This is called the "negative phase," and may last for a few hours or for many days. The degree of the reaction depends on the size and virulence of the dose and the resistance of the patient. As a rule, in twenty-four hours the patient passes into the so-called "positive phase," the duration of which is variable.

It has been found that some people were very susceptible, and that reactions, both local and general, were much more frequent than is generally supposed. When treating diseases of the upper air-passages, therefore, one must be careful of the so-called negative phase. The following is a rough guide to doses—

With influenza, streptococcus, pneumococcus, coliform, diphtheria group and coryza the primary dose of vaccine should be 1 to 5 millions; with Friedlander and catarrhalis 5 to 10 millions; with staphylococcus 10 to 25 millions.

The doses should be increased gradually if the first reaction is not too marked. At least six to eight injections should be given at regular intervals of about a week. To get a patient rapidly under the influence of vaccine, increasing doses are given on three succeeding days (Fornet and Müller). This is a safe method when starting treatment, as it is possible to inject a small first dose and then to increase it if no reaction is obtained. With smaller doses, shorter intervals than a week are required. In many instances it is necessary to continue treatment for long periods with gradually increasing intervals, because the duration of immunity varies greatly with different patients. For instance, one person may be cured of colds with a few doses and remain immune for years; another may need treatment to be repeated every winter; rarely, a good result is obtained after a long course lasting one to two years.

I have made it a general rule to continue a vaccine treatment for so long as I was convinced that the patient was better, but a word of caution is necessary. After a course of vaccines, whether the patient is better or not, the secretion should be re-examined, because there is sometimes a definite change in the infection, and in this case it is necessary to make the vaccine correspond. There seems little doubt that some organisms are more difficult to dislodge than others, *e. g.* influenza, which is more persistent than catarrhalis.

The injections should be made into the subcutaneous tissues of the outer side of the forearm or the back of the arm above the elbow. In women the back of the shoulder or the lateral side of the thigh may be preferred. Care should be taken that the syringe is sterile and that the injection avoids the main cutaneous nerves.

[For details concerning sensitised vaccines, see article on *Vaccine and Serum Therapy*.]

General Considerations

Reaction. *At Site of Injection.*—Slight swelling and redness and, later, tenderness and stiffness of the parts injected are the normal conditions after vaccination. These signs usually disappear after forty-eight hours. It is by no means uncommon, however, for local reactions to be more severe, and acute inflammation may be caused and last for several days. Rarely, an abscess forms but only after sensitised vaccines.

Local Condition.—Patients often complain that their symptoms are worse. Thus in cases of sinusitis the discharge may be definitely increased for a short time. It has been said that a sharp reaction of this kind is a favourable sign, but there is little evidence to prove it.

General Condition.—Lassitude, slackness, and a slight degree of malaise often follow within twelve hours of injection. The next day there may be a feeling of exhilaration, which tends to make the patient confident of success. In many people vaccines serve as a general tonic. I have found that a small dose of staphylococcus makes one energetic for several days. The same result is not obtained by injecting saline.

Dangers.—What is the danger of vaccines? The question is asked repeatedly by doctors as well as patients. Most of us have a natural dislike for germs; a few people obstinately refuse to have them injected.

Vaccines have been accused of causing disastrous results, but the cases are difficult to find. Doubtless there is real danger, especially in acute diseases. I feel convinced that we do not yet know to what extent and to what

lengths it is safe to give this treatment. I am always nervous about sending vaccines to a general practitioner who has no experience. I must confess that I have seen no case which was permanently worse after inoculation, but slight difficulties and complications are often met with. Even then it is hard to decide how much is *propter hoc* rather than *post hoc.*

It has been found that lassitude, faintness, nausea, and colds in the head are fairly common results. Epistaxis is occasionally caused, but anything else is rare. Instances have occurred of high temperature (4 cases), mental depression (common in slight forms), inflammation of glands (2 cases), of ears (2 cases of middle-ear suppuration forty-eight hours after vaccine), of joints (1 case), of skin (especially a return of some old skin eruption such as urticaria), of nerves (2 cases of severe neuritis), of eyes (1 case of recurrent iritis), of abdominal inflammation (*e. g.* return of gastritis or colitis), of jaundice (1 case), which were probably due to vaccines. There have been very few instances of later complications, but two cases had a return of their phthisis, one suffered from erysipelas, one from carbuncle, and one from double pneumonia, within three months of treatment.

Failures.—Doubtless a fair proportion of failures is due to our ignorance about the whole question. There is still much to be learnt about the causes of air-passage infections, and it is to be hoped that vaccines will help in the solution of the problems. Until more is known it is impossible to avoid giving wrong vaccines and wrong doses. It is often difficult to determine how long the treatment should be continued, and many people have neither the confidence nor the patience to persevere. It is now known that similar vaccines may have different curative values; and, apart from such considerations, it must be remembered that in diseases of the upper air-passages the organisms concerned are chiefly situated in the secretions on the surface of the membranes, and are, therefore, to some extent removed from the immediate action of the blood and lymph.

Results that can be Obtained with Vaccines.—To determine what results can be obtained with vaccines it is essential to approach the question from at least two standpoints. We want to know first whether better results can be obtained with some diseases than others, and secondly, whether vaccines of different types give variable results. If these differences can be proved it will help to solve our difficulties. Unfortunately our bacteriologists are too enthusiastic, and there are some people who seem totally unable to distinguish whether their patients are better or worse. The patients often expect too much, and say they are better, although the local condition is unchanged. It is natural to think of faith-healing, and doubtless a vaccine is as good in this respect as a bottle of medicine. Personally, I believe that vaccines have definite curative value in some affections of the upper air-passages; that as a general rule they are more successful in cases with intermittent periods of good health than with persistent infections such as chronic sinusitis or bronchitis where gross changes have taken place in the mucous membranes; and that with them it is easier to improve the general health than the local condition of the patient.

Acute Septic Infections.—To obtain a successful result in an acute septic infection large doses should be given early and repeated as quickly as possible. I believe that these requirements can be met better since the introduction of sensitised vaccines, because the latter are less likely than non-sensitised preparations to make the patient worse.

Of three cases treated with killed sensitised vaccines in my department at St. Bartholomew's Hospital by Gordon, one was that of a man who had submitted to an operation on his septum and tonsils. Seven days later he had acute middle-ear suppuration and his drums were punctured. On the ninth day my colleague Scott performed a Schwartze operation on his mastoid, which was found to contain a pure streptococcus infection. On the eleventh day he appeared generally septic with signs of early meningitis. We were both afraid that he would die. The next day he seemed worse and 50 millions of sensitised streptococci were injected. Within a few hours he was definitely better, and sat up and ate his food. One hundred and 500 millions were given on the next two days. On the fourteenth day he was practically well. His temperature chart showed a drop of one degree after each injection, a result also observed by Gordon in other cases. There seemed little doubt that the vaccine had saved the patient's life.

Shortly afterwards one of our house-surgeons was ill with acute inflammation of the tonsils and pharynx. The infection was very severe and was followed by cellulitis of the neck and laryngeal obstruction. On the third day his neck was incised and tracheotomy and further incisions were necessary four days after. Sensitised streptococcus vaccines (50, 100, 500 millions) were given on the fifth, sixth, and seventh days. The temperature gradually fell and was normal seven days later. The tracheotomy tube was removed on the twelfth day. Although this case is not so convincing as the former, the recovery was very good, and probably the vaccine helped.

A third case, under my colleague West, had a radical mastoid operation with drainage of

extra-dural abscess. Four days later the transverse sinus was explored, but was not thrombosed. The next day the cerebellum was explored, but no abscess found. Three days later streptococci were present in the blood, and he was given sensitised vaccines in doses of 50, 100, and 500 millions. The next day temperature was normal, and rapid recovery ensued.

In this connection it should be stated that West has treated two other ear cases, both suffering from transverse sinus thrombosis and desperately ill, with anti-streptococcic serum and sensitised vaccine, with no effect. Both patients died. It is yet too early, therefore, to say how much these inoculations will help us in the treatment of acute infections of the upper respiratory tract.

"Colds." Rhinitis, Pharyngitis, Laryngitis, Tracheitis, Bronchitis

1. **Acute Infection.**—I have treated a large number of these infections in the last four years, the majority with catarrhalis, pneumococcus, or influenza vaccines, or combinations of these. Coryza cases have not been so common, and other organisms have been rare.

The vaccine should be given early, if possible within the first twenty-four hours. By injecting myself with a single dose (5 millions each) of catarrhalis, pneumococcus, and influenza vaccines, as soon as the severe symptoms commenced, I have succeeded in curing my last three bad colds, and the attacks have been completely relieved in twenty-four hours. From the second day onwards vaccines must be used with great caution; after the sixth day they are less likely to upset the patient, and cases of copious discharge of ten days' duration can sometimes be cured rapidly by small doses on two or three successive days. It should be a rule never to give a large dose to a patient with a severe cold.

During recent years there have been epidemics of severe colds followed by irritating cough and expectoration lasting for several months. Such colds have affected adults as well as children, and have caused many a sleepless night. Sickness has been a common symptom in children, and asthmatic attacks in men. Pneumococcus and catarrhalis have been the prevalent organisms. Such cases do well with vaccines, but everything else has failed.

There seems to be abundant evidence that vaccines will often cure a cold, and the question naturally arises whether they should be used for preventive inoculation. When it is known that a severe epidemic, say of influenza, is prevalent in a town, and the facts have been proved by bacteriological examinations, the general practitioner should have his stock ready, and, as soon as one case is affected, he should not hesitate to inoculate the rest of the household. Some of his patients will be protected, others may have the disease slightly—none of them will be any worse.

2. **Chronic Infections.**—Vaccines have also been given to many of my patients suffering from severe intermittent infections of their upper air-passages. Such cases are common and present a remarkable similarity in their histories. The patients complain of having had colds for many years or all their life; that their attacks last for weeks and recur at frequent intervals; that they get their colds regardless of exposure, more frequently in the winter; that they know when a fresh attack is coming because of unpleasant sensations; many of them are slightly feverish in the early stages of each attack, and some of them are suspected of tuberculosis. The fact that sinusitis never occurs in this group is of great importance and difficult to explain.

It has been found that in many of these cases the prevalent infection was influenza, pneumococcus, or catarrhalis; that coryza is very rare; that Friedlander's bacillus, diphtheroids, streptococci, and staphylococci are of little practical importance; that it is the rule for the same organisms to reappear with each succeeding cold; in other words, that they are very persistent. That the majority of cases fall into two main groups: (*a*) influenza, commonly combined with pneumococcus; (*b*) pneumococcus and catarrhalis, constantly found together. That vaccines have a definite curative value and give markedly better results than are obtained with cases of sinusitis, presumably because of the intermittent periods of normal health which occur in the former class.

Thus, of fourteen cases with influenza infections, definite improvement was noted in eight; and still better results were obtained in the pneumococcus and catarrhalis group, eleven out of fifteen receiving benefit. That the sense of smell and taste may return even in cases which have had none for many years. That a fair proportion of the patients were highly susceptible to vaccines and were unable to tolerate the ordinary doses.

Post-Nasal Catarrh and Deafness.—My experience of vaccines in post-nasal catarrh and deafness has been limited, but my impression is that it is easier to improve the catarrh than the deafness. Very rarely a patient will say that he has heard better for a time. West states that: "Friedlander infections seem to do well, and catarrhalis quickly disappears . . . staphylococcus aureus seems to be a

favourable case for vaccination, and streptococci certainly diminish or disappear in some cases. On the other hand, the pneumococcus has so far defied my efforts . . ."

Asthma and Hay Fever.—It is not within the scope of this paper to enter into a discussion on the results that can be obtained by vaccination in cases of asthma and hay fever. My experience is limited to those cases which were associated with infections of the upper air-passages, and it has been found that when the rhinitis and bronchitis improved with vaccines the asthma and hay fever were less severe. There seems to be conclusive evidence that inoculations will in some instances protect a patient from asthmatic attacks, and the same is true to a less extent with the secondary infections of hay fever.

Furunculosis.—Four cases of furunculosis affecting the vestibule of the nose, and skin of nose and face, have been treated with staphylococcus vaccines and all improved.

Glands in Neck.—In 1911 a patient was sent to me with numerous glands in the neck which on section appeared to be lymphadenoma. He was found to have a muco-purulent discharge in his nose and the prevalent organism was staphylococcus aureus. A vaccine was prepared and given in doses of 10 to 200 millions by Dr. C. R. Stewart, who reported in June 1913 that "the vaccines undoubtedly relieved to a great extent the rhinitis, which was thought possibly to account for the enlarged glands. The patient also had a course of X-rays and the glands have gone down markedly but return at times."

Sinusitis, Acute.—A few cases of acute sinusitis have been treated with vaccines of streptococcus, influenza, or pneumococcus. Since most of these cases recover quickly, if treated early by a specialist, it is difficult to determine the exact value of inoculations. I believe, however, that streptococcus and pneumococcus infections can often be cured more quickly by vaccination than any other method, and I have no doubt that sensitised vaccines are of great value because it is possible to give a succession of large doses in a short period without affecting the general health. Influenza vaccines, on the other hand, are very depressing. They should be used cautiously and in small doses on three successive days. With this method rapid improvement has been obtained with them.

Sinusitis, Chronic.—A large number of cases of chronic sinusitis have been treated with vaccines for varying periods. In most instances there was a long history of suppuration, and other treatment such as operations had failed to cure. These persistent discharges were more often due to infections with influenza, streptococcus, and Friedlander's bacillus, than other organisms. The same organism was often prevalent in each case for long periods. Mixed infections were more common than pure. In many of these only two organisms were prevalent at one time. In some instances the combination changed. Influenza and pneumococcus were more persistent than any other combination.

Mixed infections with more than two organisms present in quantity were not often selected for treatment because the bacteriology varied with different examinations, and it was difficult to determine the exact nature of the infection.

Cases with stinking discharge in the maxillary sinus were never inoculated because they invariably did well with operations.

Catarrhalis and coryza were considered of little clinical importance because they rarely persisted long enough to require vaccines.

I have had little experience of other organisms such as diphtheroids apart from atrophic rhinitis.

I have made it a rule to use vaccines containing as few strains as possible with the idea of ascertaining whether better results can be obtained with some vaccines than others. My conclusions are as follows—

Streptococcus vaccines gave fair results. Six of nine cases were definitely improved. The same is true of Friedlander vaccines, as three out of six did well.

Of pneumococcus vaccines it is rather difficult to speak. Two patients out of six recovered, but both had recent infections. The cases with long histories were not improved at any time. It seems possible that better results may be expected by treatment with sensitised strains.

Influenza vaccines were useless. Eleven cases were treated and no good result was obtained. Such infections are most difficult to cure with any treatment; operations are rarely successful. I regard the influenza bacillus as the worst and most persistent infection of the nasal sinuses.

Staphylococcus and coliform vaccines (two cases each) were valueless, but all four patients had poor general health and very advanced disease in their sinuses. Lastly, of five cases treated with mixed vaccines three seemed less susceptible to colds.

It appears, therefore, that chronic sinusitis can rarely be cured by vaccines. I am unable to explain why better results were obtained with streptococcus and Friedlander's bacillus than with other organisms. Possibly these infections are less persistent.

A remarkable effect is sometimes obtained with sensitised streptococcus vaccines. A patient came to my hospital with purulent discharge

from her antra and fronto-ethmoidal cells of many years' duration. Her antra were drained, but the discharge did not improve. She was then given vaccine, and forty-eight hours after the second dose (25 millions) the discharge completely ceased in the left nasal fossa. A third dose of 100 millions was injected in due course, and seven days later it was found that the suppuration in the right side had almost disappeared. She remained well for three months and then went to Canada.

A second case had had repeated operations on the septum and nasal sinuses. During the past year she had used thirty to forty handkerchiefs regularly every week. She had headaches and very poor health. She was suffering from a streptococcus infection of all the sinuses. After the second dose of sensitised streptococcus her discharge was suddenly reduced so that she only required one handkerchief a day. Her headaches were slightly better and the improvement lasted for nine weeks. She did not return, however, for two months, when four more doses were given with no effect. Six months later the same infection was present and the vaccine was tried again. After the second dose the discharge immediately lessened and once more her health improved. This patient is still under treatment.

There have been no other cases in which a similar result was obtained, but one cannot fail to be impressed by the effects produced in these two instances. Moreover, we have had several cases of acute streptococcic tonsilitis which were cured rapidly by sensitised vaccines. These patients stated that they felt better within a few hours of injection and their pain and temperature improved almost at once.

I must again draw attention to the great susceptibility of these patients, especially to influenza vaccines, which are often depressing. It is easy to exacerbate the discharge with large doses, and there is no evidence to show that marked reactions are followed by a corresponding improvement in the sinusitis. On the other hand I know of no case which was made permanently worse by inoculations.

Atrophic Rhinitis.—The true cause of this disease must still be regarded as doubtful. In a series of fourteen cases the most prevalent organism was a Friedlander bacillus which was found in every case, and which grew with such ease and rapidity that other forms were overshadowed. Influenza was present in five cases, pseudo-diphtheria in four, streptococci in two, and staphylococcus aureus in only one. Almost without exception the infections appeared to be mixed and two or more organisms grew freely with each examination.

The results of inoculation with the different autogenous vaccines have been completely unsatisfactory in spite of the fact that doses from 10–1000 millions were employed and treatment was continued in some cases for many months. In only two was there any real improvement in local conditions, and this was probably due to other treatment given at the same time. In most cases treatment was not continued for long periods, because there was no sign of any improvement, and eight of the patients were distinctly upset and complained of various symptoms including lassitude, colds in the head, exaggeration of headaches, faintness, sickness, and abdominal pains. It is interesting to note that gastritis or colitis was complained of by several patients, and one of the series refused to continue the treatment because it made her colitis worse. When Friedlander vaccine has been used for other conditions it has not caused similar toxic troubles. Although the series is not a large one, there has been nothing to make one believe that this vaccine has any curative value in atrophic rhinitis. Recently, a new organism has been discovered, namely the bacillus of Perez, which is supposed to be the cause of this disease. Vaccines of this bacillus have been tried in different countries and good results have been claimed.

Vaccines before Operations

When an operation on the upper air-passages is followed by general septic infection of the blood or by cerebral complications the result is due in most instances to streptococcus or pneumococcus invasion. It occurred to me, therefore, that attempts ought to be made to immunise my patients before undertaking serious operations upon them.

In this connection it is now generally recognised that many animals can be protected against infections of various kinds by protective vaccination, and I decided to make experiments to see whether similar results could be obtained in men. One of my first patients was a man who had eight operations in India for a persistent suppuration of the frontal sinuses. I performed a Killian operation on the right frontal sinus, and gave 50 millions streptococcus vaccine twenty-four hours later. His wound healed slowly, and the temperature remained above normal for ten days. Six weeks later a similar operation was performed on the left side, but a dose of 100 millions had been given twenty-four hours before. This wound healed rapidly and the temperature was hardly raised. The after history is interesting; on the left side the result was excellent, but the right did not do well. The discharge persisted, and the patient complained of headaches from time to time. The case impressed me so much that I determined to make further investigations, and

shortly afterwards another case came to me suffering from streptococcus infection of the frontal and antral cells. This patient was carefully prepared by vaccines previous to his Killian operation. The result was most successful, and there was rapid cessation of discharge. Since then I have made it a rule to give vaccine or serum to any patient before undertaking a major operation. Of five patients with malignant growths in the jaw or larynx, four have done uncommonly well; the fifth, a case of carcinoma of the larynx, had a septic wound and secondary hæmorrhage eight days after operation, but ultimately made a recovery.

It remains to be seen, therefore, whether it is possible to immunise a patient temporarily, and so avoid the high temperature, septic wounds, periostitis, septic discharge, and cerebral complications which are so dangerous in these cases.

In conclusion, my impression is that we have already reached a point at which it is safe to say that vaccines have a definite curative value in some infections of the upper air-passages. The subject is intensely complicated, and there is no doubt that it must receive a great deal more attention before vaccines will be of great practical value to the practitioner.

W. D. H.

DISEASES OF THE BRONCHI

Bronchitis or catarrhal inflammation of the bronchial mucosa is a common affection; it may be divided into acute and chronic forms, the division being important, in so far as the treatment of the two conditions is, in some respects, different. The bronchial mucosa is in direct communication with that lining the nose, naso-pharynx and pharynx, and any infective process present in these cavities is liable, under favourable conditions for their development, to spread to the bronchial tubes. Furthermore, varying blood states and circulatory disturbances in the lungs are apt to favour inflammation of the bronchial mucosa.

Among the causes of acute bronchitis, the commonest is a simple extension of an ordinary coryza into the bronchial tubes, occurring in association with exposure to rapid changes of temperature. It occurs also as an accompaniment of certain specific diseases, such as measles, whooping-cough, typhoid, malaria and certain diseases of the lung, such as pneumonia. It may, or may not, be present as part of an asthmatic attack. The inhalation of irritating particles or gases may induce it. These so-called causes are to be regarded as predisposing only, the real causative factor being some infecting micro-organism.

Chronic bronchitis is most frequently met with in association with chronic affections of the lung, such as emphysema, chronic pulmonary tuberculosis, fibroid disease; affections of the heart, especially disease of the mitral valve, and of the vessels, such as general arterio-sclerosis in association with acute and chronic renal disease. Any local disease of the lung, such as pressure from an aneurysm or growth, will induce a condition of chronic bronchitis in its neighbourhood. Over-indulgence in food and alcohol is a common cause of chronic bronchitis. Certain drugs, such as iodine and bromine, are excreted by the bronchial mucosa, and in the process of excretion induce some degree of bronchial inflammation.

The close association between attacks of bronchitis and the presence of infecting organisms is plainly shown by the immunity from this disease those who live in clean and often very cold atmospheres enjoy, such as Arctic explorers. On their return to a warm, germ-laden atmosphere they usually suffer from severe attacks of bronchial catarrh.

As in the rational treatment of any morbid process it is of the utmost importance that the primary cause of the condition should be recognised, so that although we may in a case of acute bronchitis be reduced to treating the symptoms only (and indeed this is all that is usually necessary), the importance of the presence of the infecting organism must never be lost sight of, and where possible, cultures of the bronchial secretion should always be taken. The more common organisms found in association with this condition are the pneumococcus, Friedländer bacillus, streptococcus, Micrococcus catarrhalis and the influenza bacillus. The typhoid bacillus is found where the bronchitis occurs in the early days of typhoid fever.

During an attack of *acute bronchitis,* the patient's room should be maintained at a temperature of about 65° F. The air should be moist but not super-saturated. Indeed, the great use of the oft-seen steam kettle is in warming the air rather than in moistening it. It is conceivable that the steam kettle as often used is more damaging than advantageous, infants and those with weak expiratory power being drowned in their own secretions. The steam when used may be medicated with aromatics such as compound tincture of benzoin or eucalyptus. If the cough is very dry, and the secretion tenacious, the steam kettle may be used with advantage, but it should be withheld directly the secretion becomes loose. In severe cases the patient should be confined to bed and the bowels should be well opened with a brisk saline purge. A diaphoretic should be given, and in robust individuals this may be combined with small

doses of antimony in a prescription such as the following—

> ℞ Vini Antimonialis ♏ vii
> Spiritus Ætheris Nitrosi ♏ xx
> Liquor Ammon. Acetatis ʒ ii
> Syrup. Tolutani ʒ i
> Aquam Camphoræ ad ℥ i

This dose to be given every four hours.

Sweating can be increased by placing the patient in a hot pack. Plenty of fluid should be taken. Alcohol should not be prescribed unless the patient is used to it, and would miss it, and unless there are signs of cardiac failure. The "depressing expectorants," so-called, are the drugs to use in the acute stage. Ipecacuanha is especially useful. Carbonate of ammonium should not be used. The chest should be protected from draughts. There is no advantage gained by putting the patient in a so-called pneumonia jacket. Applications to the chest are old remedies and ones in which the public have very firm belief, but in the opinion of a large number of the profession they are of doubtful utility. There is something to be said for the reflex effects, induced by the application of heat or cold to the chest wall, on the bronchial mucosa. Heat and cold probably act in a similar manner. Cold is more easily applied and incites deeper inspiration. It can be applied in the form of a wet pack. It should cover the front and back of the chest and be changed at frequent intervals. Heat may be applied in the form of a linseed meal poultice. Where the heart shows signs of flagging, strychnine and digitalis should be freely used. Liquor Atropinæ in 1 min. doses every four hours is useful in checking the secretion where this is too abundant.

Chronic Bronchitis is a condition in which it is more necessary that the patient should be treated and not the disease. All cold, wet and fog should be avoided, and where possible the subject of this affection should winter in a more favourable clime than these isles offer, such as the south of France or Egypt. If the patient is unable to leave home, no effort should be spared in doing all possible to improve the general health. Abundance of fresh air and outdoor life should be enjoined. Mouth breathing should be avoided, the diet should be ample but simple—it is best to abstain from alcohol altogether. Cod-liver oil is of benefit in cold weather. Tepid and cold sponging are advisable. If the secretion is scanty and tenacious, ammonium carbonate and iodide of potassium should be given. The latter drug will often act like a charm. The use of alkaline fluids in a fine atomiser will often render the secretion less scanty.

Expectorants that may be prescribed with advantage are: terebene 10 min., creosote 2 min., copaiba balsam in 5 min. capsules. A very useful remedy is the old B.P. Pilula Ipecacuanhæ cum Scilla. Every grade is to be found between a mild case of bronchitis and bronchiectasis. For the irritating cough of chronic bronchitis, no better remedy is to be found than the linctus prescribed by the late Dr. Gee, consisting of equal parts of compound tincture of camphor, oxymel of squill, and syrup of tolu. The dose is 1 dr., and it may be repeated at short intervals until the cough is eased. The objection to the free use of this linctus is that it induces constipation and disorders of digestion. A valuable prescription is the following—

> ℞ Ammonii Carbonatis gr. v
> Tincturæ Scillæ ♏ xv
> Infusionis Senegæ ℥ ss
> Aquam Chloroformi ad ℥ i
> thrice daily after meals.

In children it is often advantageous to give an emetic (*e.g.* a drachm of Ipecacuanha wine), the bronchial tubes being reflexly emptied when emesis occurs. Any form of respiratory gymnastics is of value, and a chronic bronchitic may often derive great benefit from calisthenic exercises with Indian clubs in the fresh air for fifteen minutes daily.

Bronchitis occurring in the course of morbus cordis, gout or renal disease, will be relieved by treating the underlying cause. If expectoration is difficult it may often be helped by constricting the lower zone of the thorax with a band, thus diminishing the thoracic outlet and giving the diaphragm more room for play.

Insomnia is frequent with chronic bronchitis. It is often much relieved on the institution of general treatment. A hypodermic injection of strychnine last thing at night will often act as an hypnotic. A glass of milk sipped slowly at bedtime will often induce sleep. Alcohol will often have the same effect, but in the opinion of the writer it is best avoided in the treatment of this disease.

Paraldehyde in doses of 1 or 2 dr. is an excellent hypnotic. It has the advantage of being a mild expectorant and not depressing the heart. Its nauseating taste is its chief drawback. The bromides must be used in full doses to derive benefit from them. Opium as a routine is, of course, to be avoided, but if used the most useful form is that of Dover's powder in doses of 15 gr. Opium in any form is contra-indicated when this disease occurs in old people, in those suffering from marked emphysema and in children.

If it can be shown that there is a large predominance of one infecting organism the

resolution of the process may be considerably helped by giving small doses of a specific vaccine repeated at intervals of two days.

Fibrinous (Plastic) Bronchitis.—In this affection the bronchial exudate is coagulable and takes the form of solid casts of the bronchial tree. There is nothing definitely known with regard to its pathology. It has been found in association with a great variety of affections of the lung and heart, and with certain general diseases such as the specific infectious fevers. It occurs perhaps most commonly in the course of diphtheria and lobar pneumonia. The presence of bronchial casts in the sputum, together with the occurrence of dyspnœa and cough, are the distinguishing features. Hæmoptysis may be present. There is usually some fever, and the physical signs found in the chest are very variable. These signs are confined to one part of the lung—the signs may vary from a few râles to those of complete consolidation with suppression of breath-sounds. The finding of bronchial casts in the sputum makes the diagnosis certain. There is a great tendency for the disease to recur. Treatment should be carried out on the same lines as in a case of simple bronchitis. There is no specific for this condition. Potassium iodide in full doses may prove of great benefit. Inhalations of steam either alone or medicated with compound tincture of benzoin or creosote vapour materially assist the expulsion of the casts. Oxygen should be given where there is marked dyspnœa. Any associated disease such as morbus cordis or pulmonary tuberculosis should receive appropriate treatment.

Spasmodic Asthma as a clinical entity is to be distinguished from the symptomatic form which occurs in association with other diseases such as affections of the heart and kidney. Spasmodic asthma is characterised by attacks of dyspnœa occurring in paroxysms coming on for some apparently quite inadequate cause, and usually occurring in those with nervous instability. The attacks are accompanied by vasomotor and secretory disturbances, the mucous membrane of the respiratory passages throughout showing sudden hypersecretion. There is no exact pathology known. It often runs in families, but often there is no evidence of heredity. It frequently occurs along with other family diseases such as migraine and epilepsy. It affects the two sexes about equally; it may occur at any age, though in children it is more common in the female. It often accompanies, and is excited by, some catarrhal condition of the respiratory mucous membrane. The attack may be excited by the inhalation of some substance suspended in the atmosphere, such as pollen or dust. The mild catarrhal infection of the nasal or bronchial mucous membrane is often sufficient to excite an attack. Flatulence, constipation or indigestion may induce an attack. Climate and season have a varying influence, some patients being well only when living by the sea, others only in the country air, and yet others only when in the smoke and dust of the large towns. A case may be quoted of the physician who had two asthma patients under his care, the one complained that a smoky chimney brought on an attack, the other took steps to make his chimney smoke because he said that was the only way in which to get relief ! In a typical attack of spasmodic asthma the diagnosis is seldom in doubt. It is paroxysmal and sudden in onset. The expiratory dyspnœa of prolonged expiration, the fixed chest in a position of expiration, are all characteristic. Curschmann's spirals and Charcot-Leyden crystals, together with eosinophiles, are frequently found in the early sputum. The attacks are rarely, if ever, fatal.

Asthma is a capricious disease, and as such requires very varying treatment. Every drug in the Pharmacopœia has at one time or another been proclaimed as a cure for asthma. Treatment should be directed, as far as possible, towards the finding and removing of the exciting cause. Any focus of catarrh or deformity in the mucous membrane of the nasal cavities, larynx or trachea, should receive appropriate treatment. The teeth, stomach and digestive organs must be carefully regulated. The regular use of cold sponging or cold baths may be of much benefit.

The paroxysms may be so great that prompt relief is necessary. There is but one drug which commands the situation, that being morphia. A hypodermic injection of $\frac{1}{6}$ gr. will relieve the attack almost at once. The injection may have to be repeated. If there is much bronchial secretion present, and especially if accompanied by emphysema, morphia may be highly dangerous. A grave objection to the use of morphia is the institution of the habit. It should, therefore, never be used excepting in extreme urgency. According to Brodie and Dixon, atropine should be an effective remedy in relieving pain. It should be given in doses sufficiently large to produce a physiological effect. Inhalation of chloroform or ether are very efficacious, but the relief afforded is but transient. Nitrite of amyl gives temporary relief; heroin may be used as a substitute for morphia. Cocaine also is efficacious as a hypodermic injection. None of the above remedies should be left in the hands of the patient. They should always be given by a trained nurse or by the medical attendant himself.

Inhalations and fumigations are largely used. A very good powder is the following—

Potassium nitrate,
Lobelia in powder,
Powdered Stramonium leaves,
Anise fruits in powder.
Of each one ounce.

Dissolve the potassium nitrate in 1 fl. dr. of water, mix thoroughly with the powder and dry. One drachm of the above is set fire to and the fumes inhaled at frequent intervals. This remedy will be found efficacious in the majority of cases and may be left in the hands of the patient. Many of the proprietary preparations on the market have the above as their chief ingredients.

Alcohol must be mentioned as a remedy, but the risks involved in prescribing it are obvious. Hot rum and milk, hot whisky water and lemon are very useful forms. Where the attack is incited by a large or indiscreet meal, it may often be cut short by the induction of vomiting. The inhalation of steam is often efficacious and should be resorted to if no other remedy immediately offers. Vapourised iodine is a very useful remedy. It may be used in the form of a spray, the iodine being dissolved in potassium iodide and acetone in such proportions that free iodine is present.

Spirone is a preparation on the market which has the following formula—

Acetone 40 parts
Iodine 2 parts
Hyposulphite of Potash 3 parts
Glycerine 20 parts
Water 40 parts.

One drachm of the solution is mixed with 1 dr. of water and used in the form of a spray. The patient should be directed to inhale during the spraying in order to draw the vapour into the main bronchi.

Tucker's inhaler is now so well known that it must be mentioned. Its continuous use is not to be recommended. A somewhat similar preparation is—

Atropine gr. $\frac{1}{3}$
Cocaine Hydrochloride gr. ii
Hyponitrous Acid Gas to saturation
Neboline (Oppenheimer's), to ℥ i

It is used as an oily spray.

Adrenalin in 10 min. doses of the 1–1000 solution given hypodermically is often of great value in relieving an attack of asthma. The relief afforded is only temporary.

The application of the faradic current along the line of the vagus nerve in the neck is recommended.

The two drugs which stand alone in the treatment of this disease between the paroxysms are potassium iodide and arsenic. The iodide should be given in 5 gr. doses three times daily, and its use should be continued for long periods. It may with advantage be combined with arsenic, as in the following prescription—

℞ Potassii Iodidi gr. v
Liquoris Arsenicalis ♏ iii
Aquam Camphoræ ad ℥ 1
three times a day after meals.

With regard to the locality in which to live, every patient is a law unto himself. For the most part, a dry sandy sub-soil in a pine district is found most beneficial. All possible steps should be taken to eliminate any source of mental irritability or worry.

In the intervals between the attacks the patient's life and habits should be carefully regulated, great care being taken to eliminate all possible exciting causes. The diet should be inquired into. The chief meal should be arranged at midday and all indigestible articles withheld.

In young and robust individuals very great benefit is often derived by starvation diet. The writer knows of an asthmatic who observed that the frequency and severity of his attacks bore a direct relation to the quantity of food taken. He found that the less food he took the fewer attacks he had. Finally, the plan was adopted of starving himself for ten days on end, water being the only article taken. Potassium iodide in 5 gr. doses were taken three times daily. By this line of treatment the asthma has been entirely eliminated. After such a course the return to ordinary diet must be a very gradual one. Constipation should be relieved and a high standard of general health and vigour maintained. Everything should be done to exclude attacks of bronchial catarrh. Cod-liver oil should be prescribed in cold weather. The patient's bedroom should be maintained at an equable temperature. If there is a tendency to bronchial catarrh, the temperature of the room should be raised and maintained at or about 60° F. throughout the night. It so often happens that the room is warmed at the time of retiring, the fire is allowed to go out, the temperature of the room falls about 4 a.m., the patient wakening with a severe paroxysm upon him. In cases without a tendency to bronchitis, cold air may be freely admitted, and indeed such individuals will often complain of suffocation should the window be closed.

During the intervals between attacks, regular breathing and calisthenic exercises should be practised daily.

Bronchiectasis.—Bronchiectasis was described by Laennec as long ago as 1808. This is a disease in which there occurs a more or less marked dilatation of the bronchial tubes,

localised or diffuse. Rarely the condition may be congenitally present. More usually it occurs secondarily to some disease of the lung or pleura. As a consequence of this dilatation, the bronchial secretion accumulates and undergoes decomposition, and owing to absorption of products so formed a great variety of untoward symptoms arise. The condition may occur in association with any disease of the lungs and bronchi in which the deeper structures of the bronchial tubes are involved, such as bronchopneumonia, pulmonary tuberculosis, new growth, fibrosis of the lung, pneumonokoniosis, foreign body in the lung. It is rare after a simple bronchitis in which there is catarrhal inflammation only, though a persistent influenzal infection may give rise to a condition of bronchiectasis. Clinically, a patient with bronchiectasis appears cachectic and ill. There is not as a rule any loss of flesh. Paroxysms of cough, with copious and offensive sputum, are the chief symptoms. They are most marked on rising in the morning; if the cavities are full the cough is started by some change in position which causes dislodgment of secretion. Expectoration is usually free. There may be hæmoptysis. Fever is usually absent. There is marked clubbing of the fingers. The physical signs in the lungs vary, and are in the main dependent upon the associated conditions. Death usually occurs from the supervention of some complication such as bronchopneumonia or gangrene of the lung.

Treatment should be directed towards lessening the secretion and rendering it less septic. It is obviously impossible to cure the bronchial dilatations. The patient should live in the purest air possible. This improves the general health, diminishes the amount of organisms inspired and strengthens and deepens inspiration, so that secretions are the more easily expelled.

The patient should make attempts to empty the cavities by changes in position. The body should be inclined over towards the sound side with the head lowered, thus the secretions are encouraged to drain out of the affected area, and on reaching normal ciliated epithelial lining spasms of coughing are excited and the secretions thus expelled.

Inhalations are of the greatest value. The usual substance inhaled is some form of coal-tar preparation, creosote being a very favourite remedy. A small room in the patient's house should be set aside for the purpose, all openings about the fire-place, doors, windows, ventilators being sealed off. A sufficient quantity of creosote is then heated in an evaporating dish by a spirit lamp and the fumes thus allowed to permeate the room. The amount of evaporation which is allowed to take place is regulated by the amount of irritation the patient can stand, tolerance increasing day by day. As the vapour is a strong irritant the eyes and nose require to be protected, the eyes by means of motor goggles, sealed down with adhesive plaster, and the nose by means of plugs of cotton-wool. The patient should stay in the room until the cough is sufficiently excited and secretion sufficiently profuse—twenty minutes or so. This should be repeated day by day. Under such treatment the secretion becomes less fœtid and less in quantity. The respiratory capacity is increased so that the patient is capable of greater exertion without attacks of dyspnœa; the general health is much improved. The chest may show evidence of empty cavities, the signs of which were absent before.

Treatment by intratracheal injections is another method which has for its object the rendering of the cavities aseptic. The usual injection consists of—

Menthol 10 parts
Guaiacol 2 parts
Sterilised Olive Oil 88 parts

With an intratracheal syringe 1 dr. of this mixture is injected daily, care being taken to introduce the nozzle of the syringe below the vocal folds. This is not an easy matter, but with a little practice there ought not to be much difficulty. The essential oil in the fluid partially evaporates as soon as it reaches the trachea and bronchi. The vapour freed thus acts as an antiseptic to the foul secretion, stimulates inspiration and causes the lungs to undergo a great expansion. Secretion is thus more easily expelled. Five per cent. of iodoform emulsion may be used instead of the above mixture, and it has the advantage of being less irritating. Antiseptics injected hypodermically or taken by the mouth have nothing to recommend them. Direct injection into the lung through the chest wall has been attempted, but this is not advisable.

Surgical drainage of the cavities has been tried in a few instances, but the results have been for the most part disastrous. The danger from hæmorrhage, the infrequency of a single cavity and the difficulty in localising this cavity, all offer objections to this method. If the cavity lies near the surface and the lung is fixed to the chest wall by dense adhesions, surgical interference is justifiable.

Attention should be paid to the general health.

The pathology of the condition should always be investigated. The number of organisms which have been grown from the secretions of bronchiectasis is legion. Among the more common ones are the streptococcus, staphylococcus aureus, Friendländer's pneumo-bacillus,

Micrococcus catarrhalis and many non-pathogenic varieties. Rarely the Bacillus coli has been found; the pneumococcus does not commonly occur in the old-standing cases. With regard to the value of specific inoculation, there is no doubt that if it can be shown that one organism largely predominates in the secretion, specific inoculation will help; the doses should be gradually increased until quite large ones are given.

Vaccines in the treatment of bronchiectasis have been, and are being, severely criticised as an effective therapeutic measure. This is largely due to the careless administration and to the fact that due emphasis is not always laid upon the value of inoculating only when there is one largely predominating infection present.

The teeth and digestive organs should be kept in the best order possible, and throughout the colder months of the year cod-liver oil should be taken. All excesses and fatigue should be carefully avoided. For those who can afford it, the dry climate of Upper Egypt is perhaps the most desirable spot the world over for such a patient to winter in. In England, Bournemouth and the south coast are to be preferred. With care a patient with bronchiectasis may live a great many years.

The more diffuse the process causing dilatation, the more dangerous, so that the more favourable cases are those resulting from some localised condition such as pleural effusion or a localised inter-lobar empyema. H. P.

DISEASES OF THE LUNGS

Bronchopneumonia.—This disease consists in the combination of acute bronchitis and bronchiolitis with inflammation of some of the alveoli of the lung. In a few cases it is a primary disease, due to the *Diplococcus pneumoniæ*, and resembles lobar pneumonia in its course and in the treatment it requires (see *Pneumonia*). But in the large majority of instances it is secondary to bronchitis, and caused by the spread of an already established inflammatory process from the bronchi to the bronchioles and thence into the alveoli. The alveolar consolidation that results is always associated with a good deal of alveolar collapse, due to inflammatory blocking of a number of the smaller bronchi and the absorption, by means of the blood-stream, of the air contained in the alveoli to which they lead. In consequence it is often impossible to say at what point, in the course of an attack of acute bronchitis that turns to bronchopneumonia, the transition from the one to the other is effected, or whether or no the case is to be regarded as one of capillary bronchitis at some stage of its course. In a general way the diagnosis of bronchopneumonia is made by observing a gradual increase in the severity of the bronchitic patient's symptoms, the irregular fever and the dyspnœa increasing, and by the appearance of physical signs suggesting that patches of consolidation and of collapse are present in the lungs as well as bronchitis or bronchiolitis. Bronchopneumonia is a common and very fatal disease during the first four or five years of life, often complicating the bronchitis of one of the acute specific infectious fevers, particularly whooping-cough, measles, and diphtheria. It is also common in the aged, again as a complication (often terminal) of bronchitis. It may occur at any age as the result of the inhalation of infected solids or liquids into the bronchi ("inhalation-pneumonia," "aspiration-pneumonia," considered separately below), and this is the only form of bronchopneumonia that is not rare in adolescents and adults.

The main indications for treatment in bronchopneumonia are two—

1. To facilitate coughing, and the expulsion of secretion that tends to block the air tubes and so to bring about death by asphyxia.
2. To maintain the strength and resisting power of the patient throughout an exhausting disease that is likely to last for several weeks.

The patient should be kept in bed in a room at a temperature of 60°–65° F., and given plenty of fresh air while protected from draughts. It is most important that the sick-room should be well ventilated and its atmosphere prevented from becoming stale or close; to have the patient in bed out of doors is an excellent plan when the weather permits. The bed-clothes should be light but warm. Poultices applied to the chest and back have often been recommended, but have the disadvantage of being heavy and close-fitting, and so tending to cramp the respiratory movements. Anything that interferes with the free play of the lungs in bronchopneumonia is bad for the patient, and loose cotton-wool or Gamgee-tissue jackets are, therefore, more generally useful than poultices in this complaint. Anything that makes a child with bronchopneumonia cough and expectorate, and expands the collapsed portions of its lungs, is good, and the disturbance caused by examining and auscultating it, or by lifting it out of bed and carrying it about in the arms, often proves beneficial by bringing on a paroxysm of coughing. In the same way hydrotherapy is of service; for example, the child may be immersed in a very hot bath (4 gallons of water at 106°–108° F.) with a tablespoonful or two of mustard in it for a minute or two, then taken out, dried rapidly, and put back to bed.

Cold water may be splashed on its face while it is in the bath. A child that is less ill or stronger often benefits more by a cold bath than by a hot; the object is to increase the depth of the breathing and to slow both pulse and respiration, and the danger is lest the shock and chill of a cold bath or cold pack should enfeeble the heart's action and make the child pale, cyanosed and chilly. Hot and cold packs or alternate douches with hot and cold water are often worth trying, particularly in the cases with high fever and delirium.

The diet should be entirely in the form of liquid or slops, and every effort should be made to get the patient to take as much food as possible. It is particularly in the older patients that difficulty is experienced here, although the need for keeping up the strength is greater in the aged than in the young. Food should be given in small quantities and at frequent intervals—every two hours or less; milk, soups, broth, eggs in any form that is acceptable, mild stimulants such as tea, coffee, cocoa, and the diluter foods like lemonade, barley water, Imperial drink, may all be tried. It is generally best to give all these drinks hot, as their heat may aid the patient in getting rid of the bronchial secretion. More solid foods may be given as the appetite returns and the dyspnœa lessens. As regards alcohol, modern practice is perhaps less opposed to its employment than it was a few years ago. Most children and all old persons with bronchopneumonia are the better for alcohol, generally in the form of whisky or brandy, sometimes as champagne. A child of one may have 15 min. of brandy or ½ dr. of port wine every two hours; an adult half a pint of champagne or from 2–4 oz. of whisky in the twenty-four hours.

The drugs indicated are mainly those that promote bronchial secretion and those that stimulate the action of the heart. The following prescription gives an example of a stimulating expectorant in bronchopneumonia—

℞ Ammonii Carbonatis gr. i
Vini Ipecacuanhæ ♏ iii
Glycerini ♏ xv
Aquam Anethi ad. ʒ i.

Ft. Mist. One teaspoonful to be taken every four to six hours by a child under four; two teaspoonfuls similarly by a child from five to twelve.

In a general way the use of sedatives is to be deprecated, and is contra-indicated if there is cyanosis. But if the cough is very harassing it may be wise to add some form of opiate to the mixture, such as paregoric (Tinct. Camph. Co. 2–10 min.) or codeia ($\frac{1}{50}-\frac{1}{15}$ gr.), according to the age of the child, ceasing to give it as soon as the necessity has gone. For an adult, the prescription may read—

℞ Ammonii Carbonatis gr. iv–viii
Vini Ipecacuanhæ ♏ x
Syr. Papaveris ʒ ss–ʒ i
Aquam Camphoræ ad. ℥ i.

Ft. Mist. Two tablespoonfuls to be taken every four to eight hours.

Ammonium chloride is a useful expectorant, and may be substituted (in double the dose) for the carbonate in the above mixtures.

The use of the steam-kettle and of inhalations of medicated steam is often advisable in bronchopneumonia, and may be tried empirically and for so long as it seems to give the patient relief. It is indicated when the bronchial secretion is scanty, and should be stopped if the patient becomes cyanosed or the expectoration copious. The steam-kettle, or inhaler, should contain a drachm of Tinct. Benzoinæ Co., or a drachm of a mixture of this tincture with Oleum Eucalypti and Oleum Pini Sylvestris in equal parts, to a pint of hot water. It should not be used continuously. In the very severe cases when there is much dyspnœa, inhalations of oxygen, or of oxygen that has been bubbled through a strong solution of alcohol or brandy, and is in consequence charged with some vapour of alcohol, may be tried. But it must be confessed that oxygen inhalations often prove disappointing in bronchopneumonia, as if the gas failed to reach the alveoli of the lungs in any appreciable quantity.

Cardiac stimulants are generally necessary to maintain the action of the over-taxed right ventricle, which tends to fail from general toxæmia and want of aeration of the blood on the one hand, and on the other from obstruction to the circulation through the lungs. This is particularly the case with the aged patients, who should receive stimulation early in the disease. Digitalis should be exhibited in some form—Digalen, or Nativelle's crystallised digitaline; or strychnine—

℞ Liquoris Strychninæ ♏ iii–viii
Acidi Phosphorici Diluti ♏ xv
Inf. Gent. Co. ad. ℥ i.

Ft. Mist. For a child of two, one teaspoonful every six hours; for an adult, two tablespoonfuls three or four times a day.

In many cases the stomach is upset, and it is therefore better to give as few drugs by the mouth as possible; such stimulants as strychnine, caffeine and camphor may then be given subcutaneously. Camphor, much employed as a cardiac stimulant subcutaneously on the Continent, may be injected in the form of a 10 per cent. solution in olive oil, sterilised by

heat; or a mixture of three parts of camphor in twelve of almond oil and eight of ether may be employed for deep subcutaneous or for intramuscular injection. In either case the injection may be given freely, the patient receiving as much as 10 or 20 gr. of camphor in the twenty-four hours.

To promote expectoration in children judged strong enough to stand the treatment, emetics may be given. A drachm of Vinum Ipecacuanhæ may be given, and repeated every ten minutes until the child is sick; 5 gr. of copper sulphate may be given, and this drug is less depressing to the heart than ipecacuanha.

The after-treatment of bronchopneumonia demands more attention than it usually receives. In many cases the patient is left with a marked tendency to recurrent attacks of bronchitis, or with chronic bronchitis and emphysema. In others the resolution of the bronchopneumonia is delayed or imperfect, with the result that fibrosis of a more or less extensive amount of the consolidated or collapsed lung-tissue ensues, with its liability to the development of bronchiectasis. In others again pulmonary tuberculosis appears during convalescence. Special care should therefore be taken to fend off all these forms of weakness of the lungs so far as is possible. Convalescence after bronchopneumonia should take place in good country air, and be prolonged for as many months as may prove necessary for the clearing up of all pulmonary signs and symptoms. Breathing-exercises should be advised at first, or for longer periods in cases where regular and graduated out-door exercise is not available. Cod-liver oil in one form or another should always be given, and a tonic containing nux vomica often improves the appetite and with it the general condition. The more the child is out of doors the better; to ensure its proper clothing and prevent its being too warmly dressed and coddled in flannel will often entail severe struggles with nurses and fond parents, who seek to protect the patient from chills by overloading it with woollen garments.

Inhalation-pneumonia, also known as aspiration- or deglutition-pneumonia, follows the entry of septic matter or foreign bodies into the bronchi. Such matter may be a quantity of food or drink that has been swallowed the wrong way; water that has somehow got into the bronchi during diving or bathing; mucus, or gastric contents, or septic material from buccal or nasopharyngeal lesions, that may have been aspirated into the lungs by persons while drunk or patients under the influence of a general anæsthetic. Less often the septic material gets into the bronchi through a tracheotomy wound, or through an œsophago-tracheal fistula in patients with cancer of the œsophagus; by patients with ulceration or destruction of the epiglottis and the tissues at the back of the tongue food may be swallowed directly into the trachea. The bronchopneumonia that follows the aspiration of such materials is commonly a severe and rapidly fatal process, owing to the virulence and variety of the micro-organisms they contain. The main indication for treatment is to support the patient's strength with food at short intervals and with stimulating expectorants, in the hope that the infecting matter may be either expectorated or rendered innocuous by the patient's organised powers of resistance. Not infrequently inhalation-pneumonia turns to gangrene or abscess of the lung, and becomes amenable to surgical treatment. The reader is referred to the articles on *Gangrene of the Lungs* and *Abscess of the Lungs* for further information.

The Fibroses of the Lung.—Chronic pulmonary tuberculosis is by far the commonest cause of fibrous change in the lung, but it is not to be included among the causes of the comparatively rare condition known clinically as "fibrosis of the lung." In the same way the diffuse fibrosis of the lung met with in pneumoconiosis, the infection of the lung with dust or powdered minerals occurring in certain occupations, is to be excluded from consideration here. The condition may, therefore, be further defined by saying that it consists in an extensive and non-tuberculous fibrosis of the lung-tissue; and that it is due to arrested recovery from bronchopneumonia in over half the cases, in most of the remainder to delayed resolution of lobar pneumonia, pleurisy with effusion, empyema, and in a few instances to adherent pleurisy, prolonged bronchitis, pulmonary collapse, syphilis, and perhaps trauma. It is always a legacy left by some other pulmonary affection, and there is no reason to suppose that it is ever a primary disease. Except in some few of the cases arising from bronchopneumonia it is unilateral.

No drugs or treatment are known that will cause the absorption of the fibrous tissue deposited in the affected lung. The patient's chief complaints are two—chronic shortness of breath on the one hand, chronic cough and expectoration on the other. The shortness of breath is no doubt mainly due to the loss of active lung-tissue caused by the fibrosis, and should be combated by breathing-exercises and by a prolonged course of graduated physical exercises. It is surprising to see how successfully compensation for the loss of lung-tissue can be effected in working people with fibrosis of the lung, who have been compelled by the pressure of circumstances to earn their living by their own exertions. A second cause for the shortness of breath lies in failure of the right ventricle of the heart. This is met with either early in the case, when the patient over-exerts

himself before the heart has had time to accommodate itself to the altered state of the pulmonary circulation, and the increased resistance to the passage of the blood through the lungs, or else later and as a result of the strain put upon it by the patient's chronic bronchitis. It must be treated by cardiac tonics, of which the most important is digitalis (for example, Tinct. Digitalis 5–10 min. three times a day, one perle of Nativelle's crystallised digitalin once, or perhaps twice, a day, Digalen 5–10 min. two or three times a day), and an effort should be made to lessen the associated bronchitis.

Sodium benzoate in large doses (30–150 gr. a day) has been highly recommended for the treatment of pulmonary fibrosis; I have found it disappointing. The patients are particularly liable to attacks of bronchitis, and to the development of bronchiectasis in the fibrotic parts of their lungs; for the treatment of these complications see *Bronchitis* and *Bronchiectasis*.

Prophylaxis.—Once established, fibrosis of the lung is a very chronic, and frequently a troublesome, complaint. It is probable that its occurrence could often be prevented if greater care were taken with the convalescence of patients attacked by bronchopneumonia, lobar pneumonia, and pleural effusion, in whom resolution of the inflamed lung-tissue or re-expansion of the collapsed lung are delayed. It is highly important that these patients should not be got out of bed too soon, or sent back to school or to work while the physical signs of collapse or consolidation of the lung persist. Breathing-exercises should be given several times a day to aid the re-expansion of the affected part of the lung. Complicated apparatus of any kind is unnecessary; it suffices that the patient should stand up and breathe deeply and regularly, raising his extended arms above his head and rising on his toes as he inspires, lowering the arms to his sides and bending his knees as he breathes out. Expansion of both the lungs may be encouraged by making the patient blow water from one woulfe's bottle into another by the air-pressure raised in his lungs. Expansion of one lung can be aided by throwing on it the chief burden of respiration. This may be done by firmly strapping the sound side of the chest, and renewing the strapping when it works loose; or, more simply, and therefore better, by making the patient sit sideways in a chair clasping the back of it firmly to the sound side of his chest, thus limiting the respiratory movements of the sound side and increasing the work of the affected side, for periods of from ten to thirty minutes several times a day. When in bed he should be similarly encouraged to sleep lying on the sound side of his chest.

Emphysema consists in a permanent enlargement in the size of the lungs, with enlargement in size and diminution in number of the pulmonary alveoli, and loss of the elastic tissue in the lungs. In many cases it is due to over-use of the lungs, as occurs in patients with chronic bronchitis who cough a great deal, in glass-blowers and players of wind-instruments. In some instances of chronic bronchitis and spasmodic asthma it is due to over-forcible inspiration; and it is possible that in a few cases emphysema of the lungs is secondary to enlargement of the bony and cartilaginous cage of the thorax.

Treatment in emphysema is directed to the relief of two main complaints, shortness of breath and bronchitis. The shortness of breath is generally due to the smallness of the respiratory excursions the enlarged lungs are able to make; their vital capacity may be reduced to one or two litres, in place of the normal three or four litres, with the result that any slight extra-exertion finds the patient out of breath, unable to breathe deeply and so forced to breathe fast. The only treatment that is likely to do good here is the employment of breathing-exercises, the arms being raised during inspiration, lowered and pressed against the side during expiration in such a way as to aid the expulsion of air from the lungs. The patient should be directed to give particular attention to the expulsion of air from the lungs, as lack of expiratory power is one of the chief features of his complaint. In long-standing cases of emphysema the shortness of breath is often cardiac in origin, due to failure of the right ventricle; for the blood pressure in the pulmonary artery is much raised in emphysematous patients, as the resistance to the passage of blood through the lungs is much increased. The treatment here is to give cardiac tonics, of which digitalis is by far the best. Often the patient will be unable to lie down in bed at night, preferring to sleep in a chair with his legs down. Strychnine and small doses of morphine hypodermically (Injectionis Morphinæ Tartr. 1–3 min.) may be given cautiously in these instances, as these patients suffer much from the nervous exhaustion due to want of sleep.

The acute and chronic bronchitis to which emphysematous patients are so very prone must be treated on general lines (see *Bronchitis*). Ammonium carbonate or chloride, with or without ipecacuanha, are the drugs chiefly indicated—

℞ Tinct. Nucis Vomicæ ♏ v
Ammon. Carbonatis gr. iv–viii
Tinct. Scillæ ♏ xv
Spir. Chloroformi ♏ xv
Infusum Senegæ ad ℥ i.

Two tablespoonfuls to be taken three or four times a day. Potassium iodide (2–5 gr.) is useful in the cases with hard, dry cough and deficient secretion; Tinct. Belladonnæ (5–15 min.) in those with profuse expectoration.

In a general way, and in the intervals when they are free, or comparatively free, from bronchitis, emphysematous people are the better for taking drugs, particularly arsenic (Liquoris Arsenicalis 1–3 min.) and potassium iodide (2–4 grs.), three times a day; the latter is particularly serviceable in the cases with high arterial tension due to arteriosclerosis, or with liability to attacks of spasmodic asthma. The tendency of a patient taking small doses of arsenic for long periods to develop arsenical pigmentation, neuritis, or hyperkeratosis of the palms and soles, must not be forgotten, and both the arsenic and the iodide may be given in courses of a month's duration with intermissions of a month.

The climatic treatment of emphysema is of importance among the well-to-do, who travel long distances to avoid the rigours of an English winter. If the patient has much associated bronchitis and expectoration a warm and dry place is to be recommended, and may be found in the Italian Riviera, Sicily, Egypt. In the drier cases, where there is little expectoration, though the cough may be obstinate, a damper climate is to be advised, such as Madeira, Algiers, Pau, Arcachon, or the seaside resorts of the south and south-west coasts of England—Bournemouth, Ventnor, Falmouth, Torquay, St. Ives. Not a few emphysematous people are reduced to wintering indoors; and not a few find the climate of London, with all its faults, more suitable than any other. Individual experience is without doubt the safest guide here.

Two other methods of treatment in emphysema remain to be mentioned. One is treatment by the respiration of compressed air, the other is treatment by surgical operation. The compressed air treatment consists in placing the patient in a small room in which the pressure of the air can be gradually raised until it is from five to ten or fifteen pounds per square inch higher than the atmospheric pressure outside. This raising occupies half an hour; the pressure is maintained for an hour, then lowered in half an hour to the normal once more. The patient takes one of these compressed air baths a day, and goes in for a course of twenty or thirty of them. A constant supply of fresh air must be kept up while the bath is in use. The way in which these baths do good is disputed; in many cases of emphysema they prove useless, but in the minority the patient feels better, breathes more easily and suffers less from bronchitis after he has had them, and their good effects may persist for many months. The treatment is contra-indicated in cases with disease of the heart or kidneys, or with profuse expectoration. It is free from danger, and is always worth trying when available. The treatment of emphysema by surgical operation—Freund's operation—is more questionable. The operation consists in the removal of an inch or an inch and a half of the second, third, fourth and fifth costal cartilages on one side of the chest, or, in a few instances, on both sides. The object is to destroy the rigidity of the emphysematous thorax, and so to increase the vital capacity of the lungs; great care must be taken not to open the pleural cavity. A number of favourable results have been recorded on the Continent; the inspiratory expansion of the patient's chest has increased from ¼–1 inch to 1–3 inches in favourable cases, and the patient has been much more comfortable and less short of breath. In this country the results of Freund's operation have not been so satisfactory, and it must be regarded as still on its trial. It is indicated in patients who have very large and rigid barrel-shaped chests.

Gangrene of the Lung—a fortunately rare complaint, occurs most often as a complication of bronchopneumonia due to the aspiration of septic matter into the bronchi. It may follow lobar pneumonia in debilitated or diabetic patients, and is also met with if the putrefying contents of a tuberculous or bronchiectatic cavity in the lung by some mischance are spread into the lung by coughing. It is recognised by the copious expectoration of sputum with a penetrating and peculiarly disgusting odour, and by the presence of pulmonary elastic tissue in the sputum.

In many instances pulmonary gangrene is acute, a terminal event, occurring in the wasted victims of œsophageal or lingual cancer, of chronic pulmonary tuberculosis or diabetes. Here treatment can be palliative only. In other instances, however, it is a more chronic affair; and in yet others, those in which it is most amenable to treatment, it is strictly localised in the lung. The chief indications for treatment are both medical and surgical. Medically the effort should be made to lessen the quantity and infectivity of the gangrenous expectoration, and this may best be done by administration of antiseptic inhalations of creosote, eucalyptus oil, carbolic acid and the like. Dundas Grant has recommended the following mixture—

℞ Olei Cinnamomi ♏ v
Menthol gr. x
Ol. Pini Sylvestris ʒ ss
Spiritus Chloroformi ʒ ss
Creasoti ʒ ii.

M. Ten drops to be placed on the sponge of a Burney Yeo's inhaler, and renewed every hour.

In a few recorded instances good results have followed the intra-tracheal injection of a drachm of sterilised olive oil containing 10 per cent. of menthol, the patient subsequently turning on his side so as to aid the flow of this solution towards the gangrenous part of the lung. The subcutaneous injection of these pulmonary antiseptics has not proved successful. But the best results in pulmonary gangrene, the only results that have proved satisfactory in any but the mildest cases, have been those obtained by the use of surgical measures. Garrè's statistics show that out of 281 recorded cases of pulmonary gangrene treated surgically, 197 were cured and 84 (or 30 per cent.) died; medical treatment is said to have a mortality as high as 75 per cent. What the surgeon asks is that there should be definite physical signs localising the gangrenous area in any case that he is to treat by operation; a great deal of help here may be afforded by x-ray pictures. The surgeon's task is much facilitated if, as is generally the case, the gangrene comes to the surface of the lung; and still more if the neighbouring visceral pleura is adherent to the parietal layer in such a way as to lessen the two great dangers of infection of the general pleural cavity and the establishment of a sudden pneumothorax by the operative procedures. Exploratory puncture of a gangrenous lung is most inadvisable, as it has often caused a generalised infection of the pleural cavity. The operative treatment required consists in the resection of a portion of a rib and the establishment of free drainage for the gangrenous material pent up in the lung. The particular dangers of these operations and the precautions to be taken against them must be sought in special surgical manuals in which the necessary surgical technique is discussed.

Abscess of the Lung.—Cases of this uncommon condition may be divided into two classes according to their mode of origin.

1. In the first class are those in which the pulmonary abscesses are multiple, the so-called embolic or metastatic abscesses implanted by the blood, and arise in the course of venous pyæmia, or of malignant endocarditis affecting the right side of the heart. These cases are practically always rapidly fatal; the signs and symptoms are those of pyæmia, with increased shortness of breath, pain in the chest, and cough superadded. Treatment can only be symptomatic and palliative, because surgical relief is impracticable owing to the multiplicity of the abscesses in the lungs. In quite exceptional instances there may be only one or two of these metastatic abscesses in the lungs, and then the outlook is a shade less hopeless because the pyæmic patient may be amenable to surgical treatment.

2. In the second class are the cases in which the pulmonary abscess is single, or perhaps due to the confluence of a number of adjacent abscesses, and due to a local infection of the lung and not to a general pyæmic infection. Such may occur after lobar or lobular pneumonia, particularly after influenzal pneumonia; but the majority of the cases are the result of inhalation-pneumonia, the accidental aspiration of solid or liquid foreign bodies (such as food, drink, saliva, nasopharyngeal secretion, fragments of extracted teeth, and so on) into the bronchi, perhaps while the patient is unconscious or under the influence of an anæsthetic. If large, these foreign bodies are apt to set up an acute localised septic bronchitis at the point where they lodge; if small or finely-divided, an acute septic bronchopneumonia. In either case the condition is likely to pass on into abscess or gangrene of the lung (no clear distinction can be drawn between the two) if the infecting micro-organisms are sufficiently virulent and if the patient does not succumb from exhaustion before there has been time for the abscess to develop. In both abscess and gangrene of the lung the sputum is generally fœtid, often with a very horrible and penetrating odour; it contains larger or smaller shreds of pulmonary tissue in both conditions. Medical treatment is naturally of little avail in abscess of the lung; antiseptic vapours and inhalations (see *Gangrene of the Lung*) may be given as a palliative. Like empyema and gangrene of the lung, pulmonary abscess should be referred to the surgeon for operative treatment as soon as the diagnosis can be made.

New Growths of the Lung may be either innocent or malignant. The latter are either primary, or secondary to malignant tumours elsewhere in the body. The secondary growths are the commoner; they are habitually multiple, and are quite beyond the reach of any medical or surgical treatment at present known to us. Primary malignant new growths of the lung, with which it is clinically convenient to consider many of the primary malignant new growths of the pleura and of the mediastinum that are often found practically to be indistinguishable from them, are not amenable to medical treatment and only in the rarest instances to surgical; they comprise carcinoma, lymphosarcoma and sarcoma. The symptoms of such new growths are generally indefinite—pains in the chest and back, shortness of breath, progressive loss of weight and strength, progressive anæmia, cough and expectoration—as the growth is often situated at the hilus of the lung. For the same reason the physical signs are often late in appearing and inconclusive, though much help may often be derived from x-ray examinations and skiagrams. If the new growth is a carci-

noma originating in the wall of a large bronchus, hæmoptysis may occur and the physical signs suggesting extensive pulmonary tuberculosis may be found; or it may be suspected that the trouble is due to an aortic aneurysm compressing a bronchus. The treatment of such intrathoracic new growths must be almost entirely symptomatic and palliative; a few cases of intrathoracic lymphosarcoma have been recorded in which much temporary benefit resulted from a course of exposures to the x-rays. Recurrent pleural effusions often complicate these cases of malignant intrathoracic new growth. Hence careful watch should be kept to see that the patient is given relief by paracentesis as soon as he is inconvenienced by the accumulation of fluid in his chest. Attacks of spasmodic dyspnœa sometimes occur, and may be relieved by hypodermic injections of atropin (Liq. Atropinæ sulphatis ♏ ss–i–ii) with or without the addition of morphin (Injectio Morphinæ Tartr. ♏ ii–v).

Innocent new growths of the lung, including such benign neoplasms of the pleura and mediastinum as are apt to encroach upon the lung in their growth and so may be clinically indistinguishable, occur but rarely. They consist for the most part of pulmonary fibromas and lipomas, teratomas (or dermoid cysts) of the mediastinum, echinococcal cysts and gummas of both the mediastinum and the lung, fibrosarcomas of the pleura that are but slightly malignant; a number of other very rare forms of tumour have been described. The diagnosis is generally impossible *ante mortem*, except in the case of echinococcal cysts that may be identifiable by the use of the x-rays, or of syphilitic deposits that disappear under the influence of potassium iodide, mercury and salvarsan. Teratomas of the mediastinum have been recognised when they have chanced to burst into a bronchus and their hair-containing contents have been expectorated. As with the malignant new growths of the lung, pleura and mediastinum, medical treatment is useless, and surgical treatment is applicable only in the most favourable cases. A special word of warning as to the dangers of the exploratory puncture of echinococcal cysts may be here inserted. For details of the various operative procedures the reader is referred to the special surgical manuals that deal with the subject. The only exceptions to this rule are the syphilitic neoplasms; in many recorded instances these have yielded to antisyphilitic treatment. It must be remembered that while the diagnosis of intrathoracic new growths is very difficult, to discriminate between their different varieties is generally impossible during life. In all cases, therefore, Wassermann's reaction should be looked for, and if it is positive the patient should receive the benefit of a thorough course of antisyphilitic treatment.

A. J. J.-B.

POST-OPERATIVE COLLAPSE OF THE LUNGS

The condition to which this term is applied affects the lower lobes of one or both lungs, and consists in a partial or complete collapse, thus rendering a large amount of lung tissue inoperative. As the causation of the condition appears to be largely of a mechanical nature, it is necessary to consider the mechanism of its production. The expansion of the lower lobes of the lungs is dependent upon two factors, the action of the diaphragm and the movement of the chest wall. The latter is in turn mainly dependent upon the tone of those muscles which connect the thorax to the pelvis and spine, at the same time exercising pressure on the abdominal viscera. Without this abdominal action in the supine position with quiet respiration, the thoracic cage assumes the same position as is produced by a full and forcible inspiration or by emphysema. In the infantile chest or in the case of the adult in whom the thoracic cavity is funnel-shaped, this condition is unfavourable to the action of the diaphragm, but where the shape of the chest approximates to that found typically in cases of visceroptosis, the arch of the diaphragm is not diminished and the muscle contracts well. In patients in whom one-sided massive collapse is detected, the chest on the affected side is found by measurement to be greater than normal, and the abdominal muscles of the same side are toneless. The mechanism of the reflex which governs the contraction of the abdominal muscles in respiration is not understood. In the erect posture the abdominal muscles present a condition of tone, or, in other words, there is some continuous contraction of these muscles during the whole of the respiratory phase. It is, however, well recognised that in the supine position the abdominal muscles show either no tone at all, or very much less tone than in the erect or sitting position. The lower part of the chest dilates and the abdominal viscera therefore gravitate towards the thorax and tend to press the thoracic contents towards the head, and the diaphragm cannot contract to the same advantage. The quieter the respiration the more rapidly will this alteration develop. In such cases the upper lobe is found to be over-expanded and the lower lobe collapsed. This collapse develops slowly, but after twenty-four to thirty-six hours the following signs may be detected. The position of the cardiac impulse moves up to the fourth space, the upper level of the liver dulness begins at the fifth rib, the stomach resonance extends upwards into

the axilla, and the breath sounds become accentuated over the upper lobes, but are faint or inaudible over the lower lobes. In addition, the resonance over the lower lobes is diminished, distant bronchial breathing, altered voice sounds and some crepitations may be detected. The lower part of the thorax is already expanded to its fullest extent, and there is no increased expansion during forced inspiration. In the normal individual the condition is corrected rapidly when the sitting or standing posture is assumed, the reflex which produces abdominal tone coming into play. In some cases of massive collapse in the sitting position the abdominal muscles of one or both sides are quite flaccid and show no contraction during the respiratory phase. The reflex normally present is inhibited. These conditions of increased measurement of the affected side of the chest and associated atonic abdominal muscles have been present in all the cases of massive collapse which I have investigated.

The symptoms exhibited by these patients may be (*a*) none at all, (*b*) shortness of breath when speaking or drinking, or (*c*) attacks associated with marked dyspnœa and coughing and the expectoration of dark-coloured mucus, pyrexia developing subsequently. These latter symptoms are, I believe, entirely due to the inhalation of infected mucus (which is the material expectorated) into a part of the bronchial system previously not involved, coughing and dyspnœa resulting. In these attacks the patients attempt to sit up, and struggle for breath, the dyspnœa being temporarily very marked. The inhaled mucus may set up a septic infection of the bronchial system of the lower lobes, even producing bronchopneumonia.

From this summary it will be seen that collapse of a mild nature is a general occurrence in those who are kept in a supine position, the severer attacks being due to the presence of septic material. The prophylactic treatment, therefore, must be directed against these two factors. (1) Prior to operation every effort must be made to secure a healthy condition of the mouth and respiratory passages. (2) The anæsthetist should use his discretion as to the degree of anæsthesia to be induced when these parts are not in a satisfactory state. (3) Care must be taken that the patient be not exposed to chill during or immediately after the operation. (4) The patient should not be kept in the supine position for more than thirty-six hours after the operation, except in those rare cases when the exigencies of the operation demand it, but on the contrary ought to be encouraged to lie on his side and make spontaneous movements, such as changing his position in the bed, and taking food and liquids unaided. Raising his head brings the recti abdominalis muscles into action. He may also, as soon as possible, be supported by pillows for a part of the twenty-four hours, so raising the body to a reclining posture and negativing the effect of the upward pressure of the abdominal viscera. Tight bandaging of the abdomen has a tendency to increase the inhibition of the action of the abdominal muscles, and should therefore be avoided.

Should collapse be detected, but no symptoms have arisen, similar treatment should be ordered, and in addition the patient should be encouraged to talk. Artificial means for distending the lung may be employed, such as the "blow-bottle" for adults, or blowing bubbles for children. Support by a bandage or roller-towel firmly applied to the lower part of the chest, not to the abdomen, may be tried tentatively. Some patients are relieved by this measure, others will not tolerate the pressure at all or only for a short time.

When the severe type of attack occurs, the patient should be kept sitting or propped up continuously, and assistance to the breathing given by supporting the lower part of the chest, expiratory efforts being encouraged and assisted at intervals by bimanual pressure to the lower thorax. Oxygen may be administered at this time, and the patient should be reassured continually. The feeling of terror at the dyspnœa during these attacks is overwhelming. When indicated, strychnine and ether should be injected. The alarming symptoms may last from a few seconds to three or four hours. When these have passed off the patient should remain propped up with pillows, and if necessary support should be given to the lower part of the chest as mentioned above. The further treatment will depend upon the development of bronchitis or bronchopneumonia (for which see the appropriate section). The sitting position and frequent employment of the abdominal muscles will assist the collapsed lung to expand. When pyrexia with cough and expectoration ensues, blow-bottles, etc., should not be employed, and the patient should be kept quiet, propped up on pillows till the temperature has subsided. Otherwise, more septic material will be inhaled into collapsed areas and the infection will be increased. In a few cases the abdominal reflex is so deranged that in spite of the assumption of the sitting position the abdominal muscles do not come into play during ordinary respiration. Here, again, in the absence of fever, forcible expiratory efforts should be induced by the aid of the blow-bottle, etc. Occasionally, when the lungs remain collapsed for some weeks, deliberate puncture with the exploring needle will initiate recovery.

Some of the other unpleasant symptoms which are liable to follow operations, such as marked distension of the large intestine and dilatation of the stomach containing a considerable amount of liquid, also depend upon this flaccid condition of the abdominal wall, and may assist in promoting the collapse of the lower lobes by impeding the descent of the diaphragm. These should be treated by removing the contents of these viscera by appropriate measures, and adopting the foregoing methods.

J. C. B.

DISEASES OF THE PLEURA

Pleurisy, Dry or Plastic.—This, the simplest form of pleurisy, occurs with various degrees of severity from the fugitive pains met with in cases of tuberculosis of the lungs to instances which closely resemble acute croupous pneumonia. In the mildest cases relief of pain may be obtained by the application of some counter-irritant to the chest wall, as by rubbing with Linimentum Terebinthinæ Aceticum or painting with Pigmentum Iodi—equal parts of the Linimentum Iodi and Tinctura Iodi mixed, the application being made daily, or twice daily, until distinct reddening of the skin persists. The general treatment of the case is that suitable for pulmonary tuberculosis, open air and generous dietary, but if the pain is accompanied by any fever, the patient must be kept in bed. In cases of greater gravity, where the pain is considerable, the simplest means of controlling it is by limitation of the movement of the affected side. For this purpose a strip of lead plaster, two and a half or three inches in width, is cut, long enough to pass round the affected side, and to overlap the middle line at each end, before and behind. To ensure that it will lie evenly in contact with the chest wall it may be necessary to "nick" the lower border with scissors here and there. The plaster is then warmed till it is thoroughly sticky, and is quickly applied, while the patient holds his chest in a position of expiration so as to narrow its diameter as far as possible. In some instances pain is not relieved, and may even be increased by the pressure thus applied. It is therefore advisable to gain some idea as to the applicability of this method by first making steady pressure with the hand over the seat of pain, and ascertaining whether this is comfortable to the patient or the reverse. Sometimes a flannel roller-bandage passed right round the lower part of the chest is serviceable, but it has the disadvantage of impeding the movement of the unaffected as well as of the painful side. Poultices or fomentations applied to the seat of pain are generally useful: the addition of a little mustard to a linseed poultice makes it more stimulating. "Mustard leaves" are convenient substitutes in the absence of facilities for making and changing poultices: they should be moistened with warm water and covered with a layer of cotton-wool and a bandage. The application of a blister sometimes gives relief, the resulting vesicle being opened, and either treated with fomentations, or covered with a thick pad of cotton-wool. An application of antiphlogistine may be made as a substitute for poultices, if it is at hand: it is applied hot and covered with a layer of cotton-wool. On the other hand, an ice-bag or "ice-poultice" is appreciated by some patients: it should not be tried on old or debilitated subjects, but is useful in sthenic cases accompanied by high fever. Finally, the application of six or eight leeches, followed by fomentations, may give great relief. If the pain is very severe, and is not controlled by any of the above measures, opium in some form is necessary. It is best given as an injection of morphine $\frac{1}{4}-\frac{1}{6}$ gr., repeated in an hour's time if necessary; but other forms, such as Pulvis Ipecacuanhæ Compositus may be given if desired. In severe cases accompanied by fever, the general management of the case is similar to that in acute pneumonia. The patient is kept in bed, and given only fluid diet. The bowels should be attended to, and saline or mercurial purgatives are useful at the beginning of the trouble or at intervals throughout. During the acute stage a diaphoretic mixture, such as Potassii Citratis 20 gr., with Liquor Ammonii Acetatis 2 dr., and camphor or chloroform-water to 1 oz., may be given every four hours. As the disease subsides small doses of iodide of potassium are indicated to aid in the absorption of exudate: 5 gr. may be given three times a day, with gentian and nux vomica, or extract of cinchona, or any other tonic that is preferred. The troublesome cough, which is often so distressing in cases of pleurisy, is sometimes relieved by the local applications to the chest already mentioned, but may need the administration of a linctus. A simple linctus such as oxymel of squill, 15 min. and golden syrup to 1 dr. may be sufficient, but more often some sedative must be added, such as solution of morphine 3 to 5 min., or heroin hydrochloride $\frac{1}{20}$ gr. The syrup of Virginian prune is also a useful vehicle in place of simple syrup.

It is important to bear in mind in all cases of pleurisy, whether of the kind now under consideration or of the next variety, that a large majority of instances are probably caused by the tubercle bacillus: consequently, after the acute symptoms have subsided the patient should be treated (in default of evidence to the contrary) as being a tuberculous subject, threatened with

tuberculosis of the lungs, and should lead an open-air life in the country or at the seaside for a suitable period of time, the longer the better, and certainly until complete restoration of strength and weight has occurred. Further, since the natural termination of an inflammatory condition of the pleura is adhesion of the two layers of the membrane, with a tendency to some limitation of the movements of the chest in the affected area, exercises, gentle at first, and subsequently increasing in vigour, should be devised to assist expansion of the lungs and free movement of the thoracic wall.

Pleurisy with Effusion, Sero-Fibrinous Pleurisy.—Acute cases may set in with severe pain, needing some of the measures for its relief described above. Pain usually ceases spontaneously when effusion occurs, but fever and constitutional disturbance may continue. The general management of the case is the same as in acute plastic pleurisy. The principal question which arises is as to the advisability of removing the fluid by aspiration. The general principles to bear in mind are that the presence of a small quantity of fluid in the pleural sac is not in itself of importance; large quantities, on the other hand, give rise to injurious pressure, with collapse of large parts of the lung, and after a time such a collapsed lung becomes bound down by adhesions and incapable of re-expansion. Again, when the pressure within the pleura is great, the veins and lymph channels in its walls are obliterated and thus disabled from acting normally in draining away the effused fluid. Relief of pressure by evacuation of some part of the effusion will lead to absorption of the remainder by these natural channels. The general rules of treatment, therefore, are to leave matters to nature as long as it is safe to do so, but to tap the chest when injurious pressure exists, or when so long a time has elapsed that there is danger of permanent collapse of the lung. The existence of harmful degrees of pressure is evinced by displacement of the heart and mediastinum, and by grave symptoms of cardiac or respiratory embarrassment (tachycardia, cyanosis, dyspnœa, pain in the chest or epigastrium). In some cases of "quiet" effusion in which the onset is gradual, displacement of the heart or the presence of physical signs, showing that the whole of one side of the chest is practically full of fluid, may be the only indications for tapping. Rough general rules for judging of the need for this operation are as follows: the chest should be tapped (1) when the fluid has been present for three weeks, and shows no signs of diminution; (2) when the upper level of dulness on the anterior wall of the chest reaches the second rib; (3) when both pleural cavities contain considerable quantities of fluid; (4) when symptoms of pressure as described above are observed; (5) when the fluid is purulent (see below, *Empyema*). On the other hand, the presence of fever, indicating that the inflammatory process causing the effusion is still active, is an indication to refrain from tapping as long as possible, as it is almost certain that the exudate will reaccumulate after the pressure has been reduced by tapping. While waiting for the fluid to subside naturally, it is advisable to apply iodine paint to the wall of the chest as a counter-irritant, and small doses of potassium iodide may be given, as in dry pleurisy, to stimulate absorption. The patient's bowels should be kept well opened, and if there be no special indication for fluid diet excess of liquid nourishment should be avoided, but there is no need to make the sufferer uncomfortable by keeping him actually short of drink. If tapping be decided on, the exact spot on the chest wall selected for puncture is immaterial, so long as one is chosen where there is definite dulness, pointing to the presence of a good depth of effusion, and care is taken to avoid injury to other parts (heart, diaphragm). The most convenient position for the patient during the operation is on his back, semi-recumbent, and supported on pillows: he should be brought conveniently near to the side of the bed, so that the operator may reach the point of puncture without difficulty, but on no account be turned on to the sound side for convenience in operating. A convenient point to select is the sixth intercostal space in the axillary region: this should be safely above the diaphragm, and well out of the way of the heart on the left side. The instrument usually employed is a trocar and cannula about $\frac{1}{10}$ inch in calibre, connected by a rubber tube to a bottle aspirator. Only a slight negative pressure need be induced in this at first, as the fluid flows readily: if the flow diminishes as the withdrawal proceeds, a rather greater degree of vacuum may be needed, but it should not be pushed to any high degree. The trocar and cannula are sterilised by boiling before use, and the patient's skin is prepared in the region selected by careful washing with soap and water, followed by application of ether or any other antiseptic preferred. The nail of the forefinger of the left hand, also sterilised, is then pressed into the intercostal space, and the point of the trocar quickly inserted above it. No anæsthetic is generally required, but for nervous patients the skin may be frozen with ether or ethyl chloride spray, or an injection of cocaine may be given. When the point of the instrument is felt to be free in the pleural cavity, the trocar is withdrawn as far as is necessary, and the cannula is placed in connection with the partially exhausted bottle by turning the tap on the corresponding limb of

the aspirator. If after a time the fluid ceases to flow readily, a few strokes of the exhaust-pump will increase the vacuum sufficiently to make it run. Sometimes, however, the orifice of the cannula becomes blocked with a plug of fibrin, and the flow ceases and cannot be restored by suction. In such a case the trocar may be cautiously pushed back along the cannula so as to dislodge the obstruction, care being taken not to injure the lung. If this device fails, and a fair amount of fluid has been withdrawn, it is best to suspend the operation and wait for a few days, to see if spontaneous absorption occurs now that the pressure has been somewhat reduced. Aspiration should in any case be suspended if the patient begin to suffer from pain in the chest, or from faintness or from cough. It is unnecessary to withdraw every drop of fluid present in the pleura, as any small quantity left will probably disappear spontaneously. An average amount to remove is probably about 2 pints, though more may be safely withdrawn in some instances. After the cannula is removed, the point of puncture may be covered with a collodion scab.

Two dangers may be associated with the process of aspiration of the chest, syncope and acute œdema of the lung. The risk of fainting may be avoided by operating with the patient semi-recumbent, and well supported by pillows, and by the administration of ½–1 oz. of brandy with a little water before puncture. Œdema of the lung is due to too rapid expansion of the tissue to fill up the space left by withdrawal of the fluid. It is unlikely to occur if the operation is suspended when any sign of coughing or pain in the chest is encountered. It has been suggested that air or nitrogen should be introduced into the evacuated pleural cavity and allowed to be slowly absorbed by the circulation, so that the expansion of the lung should be as gradual as possible. This somewhat complicated procedure is not often made use of, owing to the smallness of the risk. Should œdema of the lung, which is signalised by the expectoration of large quantities of frothy albuminous sputum, occur, it must be treated by administration of stimulants, such as brandy and ether, by venesection or wet cupping, and finally by inhalation of a few drops of amyl nitrite, which tends to diminish the blood supply to the lungs by dilating the systemic vessels.

The suggestion has been made to utilise some of the fluid withdrawn from the pleura for inoculation of the patient (auto-serotherapy). Such a procedure would be analogous to an injection of tuberculin in a tuberculous case, as the effused fluid doubtless contains the toxins of the bacilli. As, however, even when the pleural cavity is pretty fully aspirated, there is always a certain quantity of fluid left to be spontaneously absorbed, this will have the same effect as a hypodermic injection of the same fluid, while if only a small quantity is withdrawn by an exploring syringe, there is a constant absorption of the fluid from the chest, the method seems to have little theoretical justification, and has not come into general use.

Purulent Effusion, Empyema.—The presence of pus within the plural cavity is ascertained by puncture with an exploring needle, and the point of puncture should be carefully noted for guidance in the subsequent operation : indeed it is well to make sure of the presence of pus by this means immediately before undertaking the actual operation. Aspiration of a purulent collection is only to be employed in debilitated cases in whom administration of an anæsthetic or a serious operation is not thought justifiable, as for example in cases of empyema occurring in persons suffering from advanced consumption. It is said that empyema due to the pneumococcus may sometimes be cured by aspiration, but the more radical operation is even here the more certain means of cure, and as it is not itself dangerous, it should always be preferred. No rules can be laid down for the site of operation, as purulent collections may be met with at all parts of the pleural cavity or between the lobes of the lungs. A general anæsthetic is usually given, but the operation may be done under local anæsthesia. The skin is cleaned up in the usual way and an incision is made over the point where the pus has been localised. If the intercostal spaces are here wide, it may be sufficient to incise the pleura through the intercostal muscles, and insert a drainage-tube, but it is generally preferable to remove a portion of rib with view to free drainage. For this purpose, the incision, 2½ or 3 inches in length, is made over the rib, and is carried through the periosteum down to the bone. The periosteum is then stripped off with a raspatory, and a piece of bone about 1–1½ inches in length is removed with bone-forceps. The finger should be inserted to break down any adhesions forming loculations in the abscess cavity, and a drainage-tube is passed in so as to reach to the bottom of the cavity, being prevented from escaping into the chest by means of a collar of gutta-percha tissue, 1½ or 2 inches in width, which lies against the chest wall, and is kept in place by a dressing of absorbent antiseptic wool applied over it. The escape of pus is free at first, but gradually diminishes as the abscess cavity contracts and the lung re-expands. The drainage-tube is gradually shortened at successive daily dressings as this process takes place. In some cases (and this is occasionally seen after withdrawal of simple serous effusions also), the lung is so bound down by adhesions that it fails to expand after the operation, and a permanent

cavity remains between the chest wall and the lung, which continues to secrete pus. In such an event it may be necessary to remove considerable portions of several ribs over the cavity, and thus to let the wall of the thorax fall in and become adherent to the lung, as the only means of filling up the space (Estlander's operation). The procedure is one of considerable gravity, and should not be lightly undertaken. If a sinus persist after the drainage of an empyema, the use of a vaccine prepared from the organisms present may expedite its closure.

In cases in which an empyema has burst into the lung, and been expectorated, operative treatment should be deferred until time has elapsed to allow of spontaneous healing. If the spontaneous drainage is inadequate, surgical interference is still necessary.

Hydrothorax.—Passive effusion into the pleural cavities occurs in some cases of cardiac and renal dropsy. It is also met with in persons suffering from intrathoracic tumours, though here the effusion may be due to irritation of the pleura, rather than to mere pressure. In the former instances it is usually preferable to endeavour to treat the general waterlogged condition by tapping the legs or abdomen first, but the pleural fluid must be withdrawn directly if it is seriously impeding the action of the lungs. In cases of intrathoracic tumour, repeated puncture may be needed to relieve pressure, as indicated by dyspnœa and lividity. Apart from such urgent indications it is best to leave the effusion alone, as it is fairly sure to reaccumulate rapidly.

Pneumothorax.—The commonest cases of pneumothorax, those which occur in the course of pulmonary tuberculosis, are not in themselves dangerous—indeed, the induction of artificial pneumothorax is sometimes recommended as a form of treatment for this disease. No treatment is therefore required unless temporary collapse or dyspnœa occur, when stimulants, such as alcohol, ether, sal volatile or strychnine may be given, and oxygen may be inhaled if it is available. If pus appear in the pleural cavity as well (pyo-pneumothorax) the collection must be treated as was indicated above in the case of other empyemas in phthisis. When, however, pneumothorax occurs in a comparatively healthy person, as from traumatism or rupture of an emphysematous bulla, the initial symptoms are invariably severe, consisting of pain, shock, marked dyspnœa and even threatened suffocation. An injection of morphine is usually advisable when the patient is first seen, to quiet the excited action of the heart and relieve distress. Stimulants may be given at the same time. Should the pressure within the affected pleura continue to increase, owing to the existence of a valvular opening in the visceral pleura, it is necessary to puncture the chest wall with a trocar and cannula, as for pleural effusion, the cannula being left *in situ* after the trocar is withdrawn and connected with a length of rubber tubing opening beneath the surface of some boracic lotion or boiled saline solution, so as to prevent the possibility of any contamination of the pleural cavity when the positive pressure is relieved, and suction may take place through the tube owing to the movements of the chest. In case of urgency, if puncture in this way be impossible, a free incision may be made through an intercostal space. After puncture the side of the chest should be strapped with plaster to restrain its movements. The opening in the visceral pleura usually closes quickly, and the air effused into the pleural cavity is absorbed.

Diseases of the Mediastinum

Abscess in the Mediastinum.—If the presence of pus in the mediastinum can be recognised, the collection should, whenever possible, be evacuated by surgical measures. If the abscess point, simple incision and drainage may suffice, but it may be necessary to remove a portion of rib or to trephine the sternum. If the abscess has ruptured into a bronchus, no immediate treatment is advisable until sufficient time has elapsed to allow spontaneous healing to take place. If it breaks into the pleura, the treatment is that of empyema due to other causes.

Chronic Mediastino-Pericarditis.—This obscure disease is not amenable to direct treatment. Symptoms must be relieved as they occur, the œdema of the legs being reduced by incisions or by the insertion of Southey's tubes, the fluid in the pleural cavities tapped whenever it accumulates to an injurious extent, the heart's action maintained by digitalis and other suitable stimulants, and general venous engorgement treated, if necessary, by venesection. If there is any suspicion of syphilis, mercury and potassium iodide may be tried: they may in any case have some small effect as absorbents.

Mediastinal Tumours.—Only palliative treatment is here possible, though in growths secondary to cancer of the breast it is well to try the effect of thyreoid extract, while in cases of sarcoma it would be legitimate to advise the use of Coley's fluid, the risks involved, and the small prospect of positive result being first explained to the patient. The use of the X-rays has been recommended, but it is difficult to believe that they influence growths thus deeply seated. For spasmodic attacks of dyspnœa morphine may be given and oxygen may be inhaled: tracheotomy is clearly useless except in rare cases of laryngeal spasm. Pain may also call for morphine, if fomentations fail to give relief. Fluid accumulating in the pleuræ must be

withdrawn when it gives rise to dyspnœa, but tapping should be deferred as long as possible, as the fluid is sure to recur speedily.

Enlarged Mediastinal Glands, Tuberculous or Lymphadenomatous.—See *Treatment of Tuberculosis and Lymphadenoma.* W. C. B.

TREATMENT OF DISEASES OF THE CIRCULATORY SYSTEM

DISEASES OF THE PERICARDIUM

Pericarditis.—There are three chief problems to be considered: the treatment of cases which do not require surgical interference; of those which require paracentesis, or incision and drainage of the sac; and of those in which as a result of pericarditis or mediastino-pericarditis there supervenes a condition of cardiac asystole with persistent ascites and other evidences of profound cardiac failure.

Rheumatic Pericarditis.—Each of these problems may arise in connection with rheumatic pericarditis. As a rule medicinal measures only are needed, but in rare cases paracentesis or incision is required, and in exceptional cases cardiolysis has been undertaken for the treatment of extensive external pericardial adhesions.

1. Rheumatic pericarditis almost invariably points to a severe infection and forms one element in a general carditis.

The great enlargement of the cardiac dulness which is so frequent in the severe cases indicates far more often the occurrence of an acute cardiac dilatation than an extensive effusion. The practical importance of this is that paracentesis should not be undertaken unless the indications of extensive effusion are very definite.

The chief indications in the treatment are rest and skilful nursing; alleviation of pain and distress; protection of the heart from any undue strain; medicinal and other measures for the treatment of the rheumatism, and extreme care in the convalescence.

In the nursing of adult patients it is well to have a bed of a suitable height and breadth for easy lifting in case the patient should be helpless with rheumatic arthritis. The nurses should be strong as well as skilful, and must pay attention to the posture that is most comfortable to the patient. The diet should be fluid, and if there is difficulty in digesting milk this should be diluted, citrated or even peptonised. Stimulants in the form of brandy or whisky are indicated when there is lividity, sleeplessness or a rapid feeble pulse. The danger of dilatation of the stomach in the severe cardiac rheumatism of adults demands careful attention to detail in the amount of fluid nourishment. Severe vomiting, a dangerous symptom, may require treatment by rectal feeding and the resumption of food by the mouth in small quantities given at short intervals.

External applications for pain, which may be both pericardial and pleural, should be adapted to the physique of the patient. For delicate children warm applications, such as antiphlogistine are useful. For the more robust, particularly if there is considerable fever, ice-bags are frequently most useful. The details are as follows: Mark out the pericardial area and use if possible two bags, so that one can be at once substituted when the other is empty. Refill about every two hours. Put nothing between the bag and skin but a thin layer of butter muslin, and pack round the bag with cotton-wool. For fixing the bag a domette vest is useful with armholes and a third hole through which the neck of the bag is passed. The vest is fastened above by a tape passing round the neck, and below by a safety-pin to a binder. Hot-water bottles should be placed near the lower extremities. The pulse and temperature are taken when the bag is refilled. Every precaution must be taken to guard against and watch for any signs of collapse. If the right heart is failing the application of leeches to the precordium, or over the liver if that is enlarged and tender, is indicated. In adult cases it may be necessary if the forcible action of the right ventricle points to great embarrassment to bleed the patient, but the routine use of venesection is contra-indicated. Blisters are of doubtful value, and that a blood-stained or fibrino-plastic pericardial exudation should be influenced by them seems unlikely. They relieve pain, but the ice-bag, medicinal measures or leeches are more effectual.

The propriety of opening the pericardium and draining the sac in all cases of severe rheumatic pericarditis, with the object of getting rid of the infective agent and its poisons, has been suggested, but there are grave objections: in the risk of the operation, the difficulty of draining the cavity thoroughly, and above all in the fact that the infection is primarily deposited in the pericardial tissues. In the present state of our knowledge it seems then inadvisable.

Medicinal Treatment.—There is a decided difference of opinion upon this point. If it is thought that the salicylates are specific antidotes, then large doses are indicated for

these severe rheumatic infections; in fact the largest possible doses that are compatible with safety. On the other hand, if these drugs are not specific, such large doses are not indicated, seeing that even if prescribed with the greatest experience and care they are liable to cause peculiar toxic symptoms of their own. Among these are intense depression, nausea, vomiting, polyuria, tinnitus, delirium, coma, air-hunger and death. The writer believes these drugs relieve pain and lower the temperature, which latter is, however, rarely an urgent feature. Accordingly, he uses moderate doses for these purposes, and if the illness is critical on account of the severity of the cardiac inflammation prefers to avoid any risk from their depressant action. He would warn against the danger of giving large doses of salicylates to delicate, fragile rheumatic children with pericarditis, and the idiosyncrasy to these drugs which may be met with even in strong adults. Those who believe salicylates are specific, use for an adult such doses as 20 gr. of the sodium salt combined with 40 gr. of bicarbonate of sodium every two hours during the day and every four during the night.

For pain, nepenthe (♏ x for an adult) combined with salicylate of soda, or a hypodermic injection of morphia, may be required, and is usually better combined with atropine. For sleeplessness and delirium, usually associated with discomfort and general misery, opiates, and morphia in particular, may be required, but chloralamide, or the bromides, or a combination of these various soporifics may be sufficient in the milder cases, particularly if at the same time a small quantity of alcohol in the form of brandy is given at night. In some cases small *repeated* doses of nepenthe or Liquor Opii Sedativus produce a general peacefulness and bring much relief, but with others the same treatment will cause troublesome constipation and nausea.

The bowels should be regulated by an occasional dose of calomel and saline, and later by the use of mild aperients. Nausea and vomiting require prompt attention. Bismuth and soda after food may cut short this complication, or it may be necessary for a while to stop all food by the mouth. In some instances a very harassing cough distresses the patient, and for this heroin may be exceedingly useful, but morphia alone may bring relief. Little help is obtained from drugs acting directly upon the heart; and inflamed and poisoned as it is the action must be rapid and feeble. Strychnine may be helpful when the circulation is failing, but its routine use in the early stage does not seem purposeful. Digitalis, if combined with bromides or nepenthe, may, if it does not upset the digestion, calm the turbulence of its action in some degree and thus steady the circulation. Oxygen relieves the lividity and sense of oppression.

The value of anti-rheumatic or polyvalent anti-streptococcal sera is not established. Although the writer has seen recoveries with this treatment, he has been disappointed with their inefficiency in the serious cases when really put to the test. In the present state of our knowledge of vaccine therapy he would venture to impress the need for caution in their use, and would employ them for the chronic lingering subacute cases, beginning with a very small dose, 1 million. The treatment is only on trial at present, and it is a grave step to tamper with the natural processes of healing in any reckless fashion where such an organ as the heart is concerned.

2. Cases of pericarditis which require surgical interference are the result of various conditions. Among the most important are unusual cases of rheumatic pericarditis, hydropericardium in renal disease, some tuberculous cases, pyopericardium and malignant disease invading the pericardium. There are two methods open to us, paracentesis of the pericardium and incision and drainage of the sac. Improvements in local anæsthesia and the greater certainty of the procedure have led to the more frequent choice of deliberate incision. There are two conditions in which it seems contra-indicated. These are passive hydropericardium in renal disease, and pericardial effusion the result of new growths. In both instances we may get a clear idea of the nature of the fluid from a previous pleurisy, and in both illnesses it is advisable to choose the simpler undertaking of paracentesis. In pyopericardium, incision and drainage are imperative and in the rheumatic and tuberculous cases incision is advisable. We must remember that the diagnosis of extensive pericardial effusion is not, as a rule, easy and is sometimes exceedingly difficult. There are several reasons for this difficulty, and among them may be mentioned in particular the frequent absence of any definite pericardial friction in the suppurative cases. Complicating factors in the illnesses, such as left pleural effusions, empyemata or pneumonia and greatly dilated heart with or without some pericarditis, and a dilated heart surrounded by an inflamed and much thickened pericardium, may both give rise to extreme difficulty. The fluorescent screen is a decided assistance, but even this in the most skilful hands may lead us astray. The diagnosis must, then, rest upon a most careful study of the history, of the physical signs, and the radiographic results. Two questions have to be answered: Is there pericarditis? Is there effusion sufficient in quantity or of a nature to demand surgical interference?

Among the indications for paracentesis or incision on account of the quantity of the exudation are the physical signs of a large effusion coupled with such symptoms as orthopnœa, cyanosis or livid pallor, rapid respiration and a pulse which is of small volume, rapid and irregular. The indications for incision and drainage depend almost entirely upon the history of the conditions which led to the pericarditis.

Paracentesis pericardii is carried out with all the precautions for asepsis, and every preparation should be made to combat any sudden cardiac failure during the withdrawal of the fluid. When the effusion is large and the cardiac dulness extends beyond the cardiac impulse, the fifth space at the left limit of the dulness may be chosen. Some prefer the fourth or fifth intercostal space immediately to the left of the sternum. Others the same, but to the right of the sternum. Each case should be judged individually in deciding this point.

Pericardotomy is entirely a surgical procedure. Some surgeons prefer the incision over the fourth to the sixth costal cartilages on the left side. Others have approached the pericardium by opening from below through the diaphragm.

3. Cases of pericarditis in which asystole is developing from extensive external adhesion to the chest wall. These cases are usually treated on the lines laid down for chronic cardiac failure. Brauer's operation of cardiolysis or pericardial thoracolysis has, however, been of considerable service in some of them. The most favourable class of case is that in which the chief cause of cardiac failure is the passive adhesion. Those in which there is multiple serositis—that is, an adherent pericardium with recrudescences of inflammation in the pericardium or other serous membranes, are less hopeful. For such an operation to be successful, the heart wall must be powerful, as shown by the vigorous systolic retraction and rebound of the chest wall and by the disappearance of œdema and other signs of asystole when the patient rests in bed. The absence of a valvular lesion is an advantage, and the importance of any such lesion as far as possible estimated. The chest wall should be resistant, and for this reason the patient is usually adolescent or an adult. Von Beck and Wenckebach's cases were exceptions, but the pliant chest of childhood must make us consider the advisability of this operation even more carefully in the young than in the adult. Lastly, though the operation may be followed by remarkable improvement, it is not curative, and the recovery is only relative. Death may occur during the operation, although such an event has been very rarely recorded. A skilled anæsthetist is essential. The operation for a skilled surgeon is not difficult, and consists in turning up a curved flap exposing the third, fourth, and fifth left costal cartilages and ribs, and removing some three to four inches of each. Trotter, in the writer's case, did not remove the deep periosteum, and four years later there had been no re-formation of the bones. It is important not to damage the pleura. In a successful case, the œdema disappears, breathlessness decreases, the liver and spleen diminish in size and there is great physical benefit. Much attention must be given to the convalescence, and the writer's case has taken digitalis for four years; when left off on one occasion during an attack of bronchitis, œdema reappeared. This boy, now a young man, is over six feet high and lives a quiet, comfortable life, when before the operation œdema would show itself if he took the least walking exercise and had spread upward to the abdomen.

A distinction must be drawn between this operation and thoracostomy advocated by Morison for cases of aortic disease, with anginal pain and cardiac feebleness in spite of hypertrophy. Morison maintains that the heart is embarrassed by the thoracic cage. Here there is no question of freeing pericardial adhesions.

Convalescence after pericarditis is always slow, for the condition of the myocardium, particularly if it is additionally burdened by a concomitant endocarditis, is always one of weakness. The rheumatic cases are more tedious than the suppurative because of the general carditis produced by the infection. At least six months of supervision and cautious testing of the strength of the heart by increasing calls upon it are needed after severe pericarditis. If there are adhesions, improvement may never reach beyond some limited degree. The general principles of the treatment in convalescence are those described under myocardial affections. F. J. P.

DISEASES OF THE MYOCARDIUM AND ENDOCARDIUM

In few departments of medicine is careful and skilful treatment of so great importance as in that of cardiac disorders, and in few is it so well rewarded. While it is true, for example, that we cannot rectify the actual lesion in the case of a damaged valve or myocardium, it is none the less true that in a large proportion of cases it is possible, by the adoption of adequate therapeutic measures, to prolong life for many years, and in most cases to save patients from much suffering. Moreover, the work which has been done in recent years in the realm of cardiac disorders has resulted in a great advance in

regard to what can be accomplished in the large class of patients who are the subjects of auricular fibrillation, a condition which now can be recognised with certainty.

A. Methods of Treatment Applicable to any Cardiac Affection

In considering the treatment of any form of cardiac disorder, it is of great importance that we should first of all understand that the seat of heart failure is in the myocardium. Formerly the chief interest in cardiac affections was centred in the valves. Latterly it has been largely transferred to the heart muscle. It is the heart muscle which is the key to the situation; for it supplies the force which carries on the circulation.

Now, if this view of cardiac failure is correct, certain points of fundamental importance with regard to the management of any case of heart disease can readily be grasped. Our objects should be: (1) to do everything in our power to keep the myocardium in the highest possible state of efficiency; and (2) to avoid everything which may add to the gravity of the already existing lesion, or embarrass the damaged heart; (3) to treat cardiac failure when this is present; and (4) to treat symptoms and secondary results as they arise.

We should focus our attention on the heart muscle. On the one hand every factor which has an influence in strengthening it should be taken advantage of, while, on the other hand, everything which may throw a strain upon it (such as muscular or mental over-exertion, or supernormal blood pressure) should be considered carefully and in detail.

General Measures

Given a cardiac affection, whether valvular, myocardial, or arterial, one of the most unfortunate things we have to face is the fact that such a large proportion of patients endeavour to live beyond the limits of the heart's power. It is of supreme importance that this should be avoided. The patient should acquire the habit of always living within the limits of the heart's strength; there should be an absence of undue muscular or mental strain. It is not enough to regulate the amount of physical exertion; the importance of attending to the amount of mental work is not sufficiently realised. Severe mental exertion, and all forms of excitement, anxiety, worry and emotional strain should be prohibited, since these use up the heart force.

On the other hand, care should be taken not to restrict the pursuits of a patient unnecessarily; otherwise he is apt to become unduly nervous and introspective. While avoiding strain, the patient may be allowed to do as much physical or mental work as the strength of his heart will permit. With regard to the amount and kind of physical exertion which a patient may undertake without harmful effects, it is impossible to lay down hard-and-fast rules, for the reason that the constitution and temperament of different patients differ enormously. It is possible, however, to enunciate a great cardinal principle, which is of inestimable service. It is that any exertion which the patient may undergo should not be attended or followed by undue breathlessness, palpitation or fatigue, a sense of tightness across the chest, or precordial pain or distress. On the other hand, any exertion short of producing these is usually not harmful. Violent and sudden efforts, such as hurrying to catch a train or bus, walking quickly or bicycling uphill or against a wind, or lifting a heavy weight, should as far as possible be avoided. When exercise is taken, it should be entered upon gradually. But, while undue physical exertion should be avoided, a sufficient amount of exercise on the other hand is in every way desirable.

As a rule walking on the flat is preferable to hill-climbing, but in some cases a carefully regulated plan of hill-climbing is beneficial. Systematic exercises are sometimes particularly useful, provided they be judiciously and carefully employed and their effects watched.

When the cardiac affection is progressive, the amount of effort, physical and mental, should be proportionately reduced. It should be diminished in such a degree as not to produce symptoms of cardiac distress.

If the patient suffers from an unduly excitable nervous system, this should be carefully attended to, and for this the bromides are often extremely useful, but their long-continued use is not to be encouraged. The ammonium salt is less depressant than the potassium salt, and may be given in doses of 10–20 gr., three times a day after food. The bromides are also of value in sleeplessness, and in cases of angina pectoris in which there is excitability or irritability of the nervous system. It is difficult to exaggerate the importance of sleep, and its amount and character should invariably be inquired into, and if there is defect in either this should be energetically and skilfully treated on the lines laid down elsewhere.

A patient with an affection of the heart should lead a quiet and carefully regulated life. Excesses of all kinds should be rigorously avoided. Over-eating and the abuse of tea, coffee, alcohol and tobacco should be forbidden. It is better for the patient to be a

teetotaller. If, however, he has been accustomed to alcohol and deprivation makes him miserable, a strictly moderate amount of light wine or well-diluted spirit with meals may be allowed. Alcohol is often of great value in tiding over a time of danger. With regard to diet, the intake of highly nitrogenous food should be restricted, because it increases the resistance in the peripheral circulation. The three meals of the day should be evenly balanced. In most cases the daily amount of fluid should be somewhat restricted. The meals should be as dry as the patient will take them, a sufficient amount of fluid being taken between meals. The food should be nutritious, if for no other reason than that the heart should be well supplied with good blood; at the same time it should be easily assimilated, and unlikely to cause indigestion. A diet of carbohydrates is bulky, and is apt to cause flatulence and hyperchlorhydria, while a diet consisting of highly nitrogenous food increases the resistance in the peripheral circulation. Therefore, while the diet should be a carefully mixed one, the albuminous element should predominate. Anything which causes flatulent distension of the stomach or bowels should be avoided; since this, by direct pressure, embarrasses the heart, and is one of the commonest causes of palpitation. Articles of food which the patient knows by experience to cause indigestion should not be taken. In the opinion of most, a salt-free diet is of value as an aid in preventing senile changes in the arteries, and in the treatment of arterio-sclerosis and supernormal blood pressure. If dyspepsia is present, it should be attended to. The patient should be instructed to eat slowly and thoroughly to masticate the food, and when necessary the teeth should receive attention in order to allow of this. As the subjects of valvular disease are liable to malignant endocarditis particular attention should be paid to the teeth and gums, and constipation avoided or treated. In order to get an efficient removal of waste products, not only the bowels but the functions of the liver and kidneys, and the action of the skin, should be regulated.

It is important to try to prevent attacks of bronchitis and other affections of the lungs. It is very necessary also to guard against rheumatism in valvular disease, especially when of mitral origin, and particularly so in children or young adults. In all cases of heart disease, prophylactic measures should be adopted in regard to the risks of infection by influenza or other intercurrent diseases. The difficulty attending the diagnosis of rheumatic carditis and the importance of this condition are dealt with in the section relating to acute simple endocarditis. An attack of bronchitis or other affection of the lungs, rheumatism, influenza, or other febrile disease should be most carefully and energetically treated, and a sufficient amount of rest during convalescence should be enjoined. When exertion is again allowed, it should not be such as will produce any symptoms of cardiac distress; if it does the amount must be diminished. Any existing anæmia requires to be effectively treated by a plentiful supply of red meat, and iron with arsenic.

Patients who exhibit a gouty tendency should have their diet regulated, and take an occasional dose of blue pill followed by a saline aperient. Colchicum in combination with alkalies, or, if colchicum is not tolerated, a suitable substitute may be administered with advantage.

Where there is supernormal blood pressure, this should be regulated on the lines laid down elsewhere.

If there is reason to believe that heart disease is the result of syphilis, the iodides are frequently of value, and should be given in full doses, 15–20 gr., three times a day for some weeks; when the syphilitic infection is recent, mercury may be combined with iodides. In adults who are the subjects of heart disease a course of such tonics as iron, arsenic, phosphorus, or strychnine may be taken from time to time; while in children cod-liver oil, the syrup of phosphate of iron, or the syrup of iodide of iron are of special advantage.

Special Forms of Treatment

Rest.—It is difficult to exaggerate the importance of rest in the treatment of cardiac failure. I have no doubt that not infrequently improvement thought to be entirely due to some other therapeutic agency is, in reality, partly or wholly the result of rest. While rest is indicated in all cases of cardiac failure, it is of considerably greater value in cases without auricular fibrillation than in those with it; indeed, in the former group of cases, rest easily holds the first place among the therapeutic agencies at our disposal.

In determining the degree to which exertion should be curtailed, a cardinal principle, as has already been pointed out, is that the exertion which the patient indulges in should fall short of producing symptoms of cardiac distress. When there are indications of progressive exhaustion of the heart's strength, the amount of effort should be proportionately reduced, and in cardiac failure it may be necessary to recommend the patient to stay in bed. In the slighter degrees, it may be sufficient if he goes to bed for a couple of hours every afternoon or stays in bed one day a week. When heart failure is marked or extreme, as, for example, when orthopnœa and dropsy are present, the amount of exertion should be reduced to a minimum,

the patient being kept in bed for a period which may extend even to some months.

Diet.—In cases of cardiac failure unaccompanied by nausea and vomiting, light solids form the best diet, and, as a rule, agree better than fluid food. The daily amount of fluid taken, particularly at meal times, should be less than when there is an absence of cardiac failure. Specific instruction should invariably be given in regard to thorough mastication, and great care should be exercised to see that the patient does not take a larger quantity of food than he can comfortably digest. The food should be easily digestible, and those articles of food which are found not to agree with the digestive organs should be eliminated. When cardiac failure is extreme, the amount of food should be considerably restricted, and only very small quantities at a time, at fairly frequent intervals, should be allowed. Occasionally a milk diet or a modified Salisbury diet is best.

In the gastric crises, with vomiting, which sometimes accompany cardiac failure, milk is in the majority of cases the best food. Sodium citrate (15 gr. to each 10 oz.) may be added. If milk is not tolerated when taken in the usual way, peptonised milk, milk gruel, koumiss, or strong meat essences may be sipped, the patient not being allowed any solid food. If koumiss is given, no other food should be given at the same time. If one of the digitalis series of drugs is indicated for the general condition, and the patient is peculiarly intolerant of digitalis, strophanthus, squills, or one of the other substitutes may be tried. A brisk purge should be administered, and bismuth and hydrocyanic acid may be given. Iced champagne is sometimes useful, and counter-irritation over the epigastrium is occasionally of some help for the relief of vomiting. If, in spite of these measures, the vomiting still continues, all food and even water and drugs by the mouth should be stopped, and rectal feeding resorted to. The great advantage of rectal feeding with milk pancreatised for at least 24 hours in these cases, is not sufficiently realised. If dropsy is present, a salt-free diet is believed by most to be of value.

Systematic Exercises.—It has been pointed out that systematic exercises are sometimes particularly useful, provided they be judiciously and carefully employed and their effects watched. Graduated exercises are of special value in cases of slight cardiac failure due to the heart muscle being flabby and lacking in tone, as in fatty infiltration. It is essential that the myocardium should be fairly sound. Exercises are contra-indicated in acute affections of the heart, in considerable myocardial degeneration, in cases of severe cardiac failure, and in cases in which the heart failure is progressive. In my opinion simple movements are, certainly in most cases, better than the resistance exercises practised at Nauheim. Exercises may be indulged in even when the patient is confined to bed. They should stop short of producing any indications of cardiac distress.

Baths and Spa Treatment.—It is commonly known that immersion of the body in water may exercise a decided influence on the circulation. Some writers also believe that certain waters at Nauheim, on account of their ingredients, possess a specific therapeutic value in cardiac affections, but I am very sceptical with regard to this. Patients undoubtedly often derive great benefit from a stay at Nauheim and at similar spas, but this is almost certainly due to the change of air, the rest, the regular mode of life and exercise, the careful dieting, and other factors. Given the same conditions of life, similarly good results would be obtained anywhere.

Massage.—Massage is useful in many cases. It may be employed in cases in which the patient is confined to bed but in which absolute rest is not necessary, while, on the other hand, ordinary muscular exercise is not advisable. Massage and bandaging of the lower extremities are frequently of value in dropsy.

Drugs.—It is, unfortunately, in all probability true that the reputation of many drugs used in the treatment of cardiac affections does not rest upon trustworthy evidence. When a combination of various therapeutic agencies are employed, we should be careful to avoid crediting the administration of any drug with results which are in reality due to some other agency, more especially rest, or to the natural course of the malady.

A problem which has been notoriously a source of difficulty and perplexity to the clinician is the extraordinary difference in the results of the administration of digitalis or one of its allies in persons who are suffering from identically the same lesions, and complaining of precisely the same symptoms. As long as the drug has been in use for the treatment of cardiac affections it has been known that the results of its administration have been astonishingly variable; in some cases of cardiac failure it is of very great value, while in others it is ineffective. As an example of this, let us suppose three patients are suffering from precisely the same degree of cardiac failure and identical lesions, and the same dosage of digitalis is employed in each case. In one, perhaps, the results are extraordinarily good, the drug seems to act like a charm; in the second, the beneficial effect may be only moderate or slight; while in the third absolutely no good result at all can be detected. What is the cause of this variability? Is the drug capricious in its action or uncertain in its strength? It has been thought so. Or, is it due to some par-

ticular preparation being active while another preparation is inert? This has been thought by some; and for this reason special preparations have been prepared and advertised as being more uniformly certain in their action. These opinions have been proved to be wrong. Put briefly, the explanation of the extraordinary difference in the results of administration of digitalis or its allies is that the response to the drug differs according to the condition of the heart and character of the rhythm; those cases of cardiac failure which show wonderfully good results being, in the vast majority of instances, cases of auricular fibrillation.

The Digitalis Series of Drugs.—Of drugs used in cardiac affections digitalis is undoubtedly the best cardiac tonic. The commonly accepted special indications for giving digitalis are increased pulse-rate, say over eighty per minute, weakness of the contractile force of the heart muscle, cardiac dilatation, and anasarca; the cardinal indication being failure of tonicity. It is more generally useful in mitral than in aortic cases, especially in cases with scanty, high-coloured urine, and with dropsy. This is easily understood when it is remembered that auricular fibrillation is much more common in mitral lesions. The drug is often very useful when mitral regurgitation has become superadded to aortic disease. It is also useful in many cases of chronic myocarditis and fibroid degeneration, but the effects should be carefully watched in these cases. The question is often asked as to whether digitalis should be given in cases of aortic insufficiency. A supposed disadvantage is that slowing of the pulse, by prolonging diastole, allows more time for the distension of the left ventricle by the regurgitant current of blood. It should be pointed out, however, that slowing of the pulse may occur independently of digitalis. It is further urged that the use of the drug tends to cause sudden death in this affection. Patients have undoubtedly been known to die during its administration, but it does not necessarily follow that digitalis is responsible, for sudden death is apt to occur in aortic disease whether patients are taking the drug or not. In order to prove the contention, there should be no doubt that a relatively larger proportion of people suffering from aortic disease die when taking the drug than in the case of those in which it is not being used. In my opinion, there is no evidence to support this view. To be on the safe side, however, the drug should be given cautiously in this condition, and the patient should be kept in bed when considerable doses are being administered, while in those cases in which auricular fibrillation is not present the drug should be stopped as soon as the acute symptoms have gone.

Digitalis is, as a rule, contra-indicated in cases of undue slowness of the pulse. In these cases, if given at all, it should be cautiously administered. It should also be cautiously given or avoided altogether when there is a forcible apex-beat and bounding arteries. It is possible to do harm in cases of diminished conduction, though the drug is not necessarily contra-indicated. In these cases, care should be taken not to diminish conduction still further. Among the common beliefs, which are held without questioning by the profession at large, is the belief that the internal administration of digitalis increases the blood pressure in man by constricting the peripheral vessels. The result of this is that therapeutists are afraid of administering the drug in cases of cardiac failure in which there is degeneration of the arterial coats, for fear of rupture of their walls and consequent apoplexy, or where cardiac dilatation is associated with increased arterial tension from disease of the arterial coats and of the kidneys. Some try to get over the difficulty by prescribing along with digitalis some depressor, such as sodium nitrite or nitroglycerine, in order to dilate the vessels and so lessen the arterial tension. It should not be forgotten, however, that the effects of depressors are but transitory, while the rise in the peripheral resistance—if it is brought about by digitalis—is practically continuous. Others prefer to employ strophanthus in these cases, because of the prevailing view that it has little or no effect in constricting the vessels. I have shown from investigations [1] that, judged by the methods in use for observing the blood pressure clinically, the drug does not raise the blood pressure in man, and, therefore, there is no risk in administering it in cases of degeneration of the walls of the blood-vessels or of supernormal blood pressure.

But while the special indications for digitalis are increased pulse-rate, weakness of the contractile force of the heart muscle, dilatation, and dropsy, the results of its administration when these are present are very variable. The remarks which I am going to make on this subject are mainly based upon a series of investigations in which I was associated with Dr. James Mackenzie, Professor Cushny, and other workers at the Mount Vernon Hospital, dealing with the action of digitalis and some of its allies on the human heart.[2]

[1] See papers in the *British Medical Journal*, Sept. 21, 1912, and Sept. 13, 1913, and *Transactions* of the Seventeenth International Congress of Medicine.

[2] See a paper entitled "Recent Advances in Cardiac Therapeutics" in the *British Medical Journal* of Oct. 7, 1911, and another entitled "Recent Advances in the Diagnosis, Prognosis and Treatment of Heart Disease" in the *British Medical Journal* of March 8 1913.

These investigations showed that the response to the digitalis series of drugs differs according to the condition of the heart and character of the rhythm. Those cases of cardiac failure which show wonderfully good results are, in the vast majority of instances, cases of auricular fibrillation—whether the lesion be mitral, aortic, or myocardial—particularly when subsequent to acute rheumatism or chorea. If auricular fibrillation is present, and is accompanied by a rapid pulse, whether dropsy is present or not, digitalis is a therapeutic agency of wonderful potency; the results in the majority of cases being very good, and in some cases extraordinarily good. If that be so, it is of the utmost importance that we should be able to recognise auricular fibrillation clinically. It may be recognised with certainty by the following: (1) The pulse is completely irregular; it is an irregularly irregular pulse. The irregularity is more pronounced when the pulse is fast. When the pulse is slow, as, for example, when the patient is under the influence of digitalis, it may be necessary to take a tracing of the radial artery and to adopt careful measurements. (2) In mitral stenosis, a presystolic bruit, *due to auricular systole*, disappears with the onset of auricular fibrillation; if a diastolic bruit was present, it persists. A word of warning is necessary here. A murmur filling the whole space between the second and first sounds may be present in cases of rapid heart action, and the latter part of the murmur is not infrequently mistaken for a presystolic murmur due to the systole of the auricle. This mistake need not be made. The murmur is not crescendo in type, and on auscultating during one of the long pauses, or when the heart's rate becomes slow, a silence will be detected between the termination of the murmur and the first sound. (3) By means of the polygraph. In a tracing of the jugular vein there is an absence of the normal *a* wave; in other words, there is the ventricular form of venous pulse. The normal *a* wave cannot be present because the auricle does not contract. Instead of the *a* wave there may be multiple undulations. (4) By means of the electrocardiograph. In cases of auricular fibrillation, the administration of the drug is followed by a rapid fall in the pulse-rate and a concomitant improvement in the general symptoms. Two exceptions are: (1) Cases of cardiosclerosis in which the degenerative change is so widespread that little healthy muscle remains, and (2) cases in which there is pyrexia. When pyrexia is present, apparently the response to digitalis, if present at all, is as a rule very slight, whether auricular fibrillation is present or not.

With regard to dosage: as a rule improvement can be started after a time by small doses of 5 min. of the tincture three times a day, but in this case a much longer period is required than when large doses are employed, when the full effects are produced rapidly. The inference is, therefore, that it is better to begin with full doses and to go on with these doses until some physiological reaction is obtained; and then, if required, to continue the administration, but to regulate the amount until it is discovered what is the optimum dose in a given case. It is well to begin with a drachm of the tincture per day, or in urgent cases with even 1½ or 2 dr. per day, and to continue until there is nausea or vomiting, diarrhœa, headache, an unduly slow pulse, or what is called "coupling of the beats."

Usually a reaction is obtained within a week, sometimes in a few days. The drug should be stopped until these symptoms have passed away, which generally happens in a few days. As a rule the patient relapses. The indication then is to find out what dose suits him best—that is the dose sufficient to control the heart and maintain the slow action without producing toxic symptoms. It is a good plan to begin with half the original dose, and this can be increased or diminished according as the rate of the heart increases or diminishes. In this connexion, help may frequently be obtained from the patient himself, who is often able to say what quantity suits him best; in other words his own sensations are often a good guide, and should be taken into account as well as the pulse-rate. It may require weeks or even months of careful observation to find this optimum, and much perseverance will generally be required. There may be wide differences in the amount required in individual cases; this may be as small as a drachm per week, or as large as 45 min. per day. Having discovered this dose, in the great majority of cases it will be necessary for the patient to continue the drug for the remainder of his life. It may be necessary to diminish or increase the dose later on. Apparently the cumulative action is not nearly of such serious account as has been supposed; at the same time the pulse ought to be watched day by day. By this mode of treatment we can save many lives, and also bring comparative comfort to people who would otherwise be the subjects of much misery.

When auricular fibrillation is not accompanied by a rapid pulse, no marked result follows the administration of digitalis; the result is scarcely greater than in cases without auricular fibrillation. The improvement is slow, and it is often difficult to be certain how far the improvement may be due to the rest in bed and other measures adopted apart from the effect of the drug.

If the case is not one of auricular fibrilla-

tion, in exceptional cases fibrillation may occur during the administration of the drug; but, apart from these cases, and also cases of auricular flutter, as a rule, though not always, the beneficial results will be only moderate, or slight, or none at all. It is well to begin with large doses here also, and to continue until there is nausea or vomiting, diarrhœa, headache, an unduly slow pulse, extra-systoles or partial heart-block. We should be careful not to diminish conduction too far. Thus when extra-systoles or partial heart-block are produced the drug should be stopped or the dose reduced. If improvement in cases without auricular fibrillation does occur, it can usually be maintained without continuing the drug. Sometimes, however, it is advisable, after stopping the drug for a few days, to resume with smaller, sufficiently large, doses to maintain the slowed action and improvement. Here also other evidence of the patient's own sensations should be taken into account.

In giving digitalis there need be no fear of untoward results provided the indications previously mentioned are borne in mind. As long as the drug is not pushed after the first indications of its physiological action appear there is no danger. We should be cautious if the pulse is below seventy per minute. "Coupling of the beats" is a danger signal. Either the drug should be stopped for a few days or the dose diminished. It should be remembered that over-dosage may cause the patient much discomfort.

There is no evidence that any of the more recent preparations of the digitalis series are, generally speaking, superior to the tincture of digitalis for ordinary treatment. In some cases *strophanthus* and *squills*, while having the same action on the heart, seem to have less tendency to act on the digestive system. On the whole digitalis appears to be more certain in its effects than either strophanthus or squills. When it is unsuccessful as a rule the other drugs are of little value. Therefore digitalis is generally the most useful drug. The others should be regarded as substitutes for digitalis, and may be tried when a patient is peculiarly intolerant to the latter on account of the production of nausea or diarrhœa.

As a rule about twice as much tincture of strophanthus or of squills is required to produce the same effect as of digitalis. There is no special advantage in the various extractives obtained from digitalis. The tincture includes all the glucosides. With regard to the so-called alleged active principles of digitalis, it should be borne in mind that there is no pharmacological or clinical evidence that they are either pure substances, or that they are more reliable than different samples of the tincture. Possibly they are not so reliable. Nativelle's digitalin granules are a convenient form. Samples of tincture of digitalis supplied by firms of chemists of repute have proved wonderfully constant in strength. It is advisable, however, whenever possible, to get the tincture of guaranteed strength. The fresh infusion of digitalis is also reliable. The preparations of strophanthus on the market are not supposed to be nearly so trustworthy as those of digitalis. It was found that the active principles of digitalis, strophanthus and squills readily underwent decomposition when the tincture was diluted with water, and this was especially so in the case of strophanthus. For this reason, the tinctures should be dispensed as such or diluted only with alcoholic preparations, with directions to the patients to take them in water if necessary. Intravenous injections of strophanthin were employed by other workers at the Mount Vernon Hospital. These injections may be used in the most acute cases of cardiac failure, when it may be desirable to elicit a more rapid effect than is possible by the administration of tincture of digitalis, or one of its allies, by the mouth. Either two or three doses of $\frac{1}{250}$ of a grain at an interval of two hours, or a single dose of $\frac{1}{100}$ of a grain, may be administered. Whenever necessary, we can continue the administration of tincture of digitalis by the mouth. Some employ hypodermic injections of digalen or digitalin (the latter in doses of $\frac{1}{100}-\frac{1}{50}$ gr.) in cases of emergency, when a more rapid effect is required than is possible by administering tincture of digitalis by the mouth.

Caffeine has acquired a reputation in the treatment of cardiac affections, but this is, in the main, the result of its diuretic action, which is of great value. Apart from its diuretic action, caffeine may be tried when digitalis, strophanthus and squills have failed in cases of cardiac weakness and failure, particularly where there is no dilatation. It does not slow the pulse, and, therefore, bradycardia is no contra-indication to its use. *Theobromine* has a more constant and marked effect upon the kidneys than caffeine. *Agurin* or *theocin-sodium acetate* is of still greater value as a diuretic. *Diuretin* is also a good diuretic; it is more soluble than theobromine. Caffeine or theobromine may be used in conjunction with one of the digitalis group. Caffeine is apt to produce restlessness and sleeplessness. The others mentioned do not.

Strychnine has a great reputation in cases of cardiac failure when very rapid effects are required, but there is no absolutely reliable experimental or clinical evidence that in medicinal doses the drug has any effect upon the heart or blood-vessels. While this is so, many are of

opinion that the prevailing belief is supported by clinical evidence. The action of the drug is probably an indirect one as far as the heart is concerned, its essential action being that of a respiratory stimulant.

Diffusible stimulants (alcoholic, ammoniacal and ethereal) are of value in some cases of heart affections, particularly during temporary attacks of cardiac failure, and for the relief of urgent symptoms. Sometimes they may be given with advantage before there is decided cardiac failure.

Alcohol is supposed to be of greater value in the cardiac failure due to acute myocarditis than that associated with valvular disease. It is often a good thing to begin with a small quantity of wine with food. Ultimately, stimulants in larger quantities are required, and of these old brandy is the best. My custom is to begin with 2 or 3 oz. per day, gradually increasing the quantity as required and never going beyond 10 oz. daily, the amount being gradually reduced as the patient improves.

Atropine is supposed to paralyse the cardiac inhibitory terminations, and cases of heart-block have been recorded in which the writers have stated that in their opinion the drug was the means of increasing the ventricular rate. If this is so, it should be of service in Adams-Stokes' syndrome. One-hundredth of a grain may be given hypodermically, and repeated in half an hour if necessary. I am bound to say, however, that I have never seen any good result follow its administration in these cases.

Some believe that *iron* and *arsenic* are cardiac tonics, and, therefore, do not restrict the use of these drugs to cases of heart disease in which there is co-existing anæmia, but employ them in the early stages of cardiac failure. It is possible that arsenic is a nervine or muscular tonic. Sir William Broadbent believed that *phosphorus* was of more value than arsenic.

The *iodides* are frequently of value in gouty conditions, in supernormal blood pressure, in arterio-sclerosis, in aneurysm, in angina pectoris, and most of all when there is reason to believe that arterial or valvular disease is the result of syphilis. They may be taken for long periods. With regard to the effect of iodides upon high blood pressure, the results of some clinical investigations which I conducted at the Mount Vernon Hospital, showed that in no case was the administration of iodide of potassium, even when given in doses of 1 dr. three times a day, followed by a lowering of the blood pressure; yet in certain cases the drug seemed to be of value. In respect to arterio-sclerosis, while iodides may exert a beneficial influence in the earlier stages of the disease, it is practically certain that they are valueless in the later stages. When arterial, valvular, or myocardial disease is the result of syphilis, and, therefore, more frequently in aortic than in mitral disease the iodides have a specific value. In these cases they should be given in full doses (15–20 gr.) three times a day for some weeks. When the syphilitic infection is recent, *mercury* may, with advantage, be administered along with the iodides.

The *nitrites* may be given beneficially in cases of increased blood pressure or in angina pectoris—in the latter even if unattended with high pressure. Nitrite of sodium, erythrol tetranitrate, nitroglycerine and nitrite of amyl are most commonly employed.

Purgatives are of value in supernormal blood pressure, and when there are indications of distension of the right chambers of the heart and dropsy.

Diuretics should be given in cases in which the urine is scanty, especially if dropsy be present.

Oxygen.—This is sometimes of value in cases of cardiac failure. The chief indications for its use are dyspnœa, cyanosis and angina pectoris, particularly the two former. On the whole, I have been disappointed with the results of its administration, though occasionally substantial good has apparently attended its use. Leonard Hill has introduced a new method of giving it, by which the patient inhales almost pure oxygen.

Blood-letting.—This is of considerable value in a certain class of cases, and I am inclined to think that this mode of treatment is often not used when it might be employed with great advantage. It should be employed when there are indications of great distension of the right chambers of the heart—as, for example, severe dyspnœa, cyanosis, noticeable turgescence of the veins of the neck, and increased area of impairment of the percussion note to the right, especially when the radial pulse is small and weak, while, at the same time, there is forcible pulsation of the right ventricle in the epigastrium. As a rule, venesection should not be performed in aortic incompetence; in these cases it often does harm. My custom is to choose the median basilic vein, and to withdraw a good quantity of blood—occasionally even up to 20 or 30 oz.; sometimes, however, 6–10 oz. is sufficient. If venesection is not practicable, or is objected to by the patient or his friends, six to twelve leeches over the right ventricle or liver are good substitutes. When blood-letting is employed, it should be accompanied by dry diet and free purgation.

Treatment of Temporary, or more or less Permanent, Cardiac Failure.—In temporary cardiac failure, the amount of physical and mental effort should be reduced. If the indi-

cations of cardiac failure are slight, continuous rest in bed may not be necessary, although it is usually better to begin treatment by keeping the patient in bed for a short time. The amount of food should be restricted, and if necessary, efforts should be made to procure sleep. If the heart failure persists in spite of these, other remedies, including drugs, should be employed, and, if indicated, symptoms should be treated.

When the heart failure is extreme, as, for example, when orthopnœa and dropsy are present, absolute rest in bed is imperative. Further restriction of the amount of food, strict attention to the condition of the bowels, and, if necessary, the employment of therapeutic measures for procuring sleep, are indicated, while drugs appropriate to the condition should be employed until the requisite effects are obtained. Special symptoms should be treated as they arise.

In both temporary and more or less permanent cardiac failure the indications for, and the manner of employment of, each class of therapeutic measures have already been fully described.

Convalescence from severe cardiac failure is sometimes aided at first by gentle massage, and later by carefully regulated and gradually increasing exercises—at first passive, and later active—before the patient is allowed to get up. The movements should always stop short of producing breathlessness, fatigue, or other indications of cardiac distress, and should be followed by a period of absolute rest.

Treatment of Symptoms and Secondary Results. Rest, and other remedies previously described in detail should be employed in the treatment of symptoms and secondary results.

Sleeplessness.—The great importance of securing an abundance of sleep has been noted. Sleeplessness is often a troublesome, and may be a very grave, symptom. It should always be remembered that sleeplessness may be due to dyspnœa, and in these cases sometimes the patient is troubled with "night starts" as he is falling off to sleep; in these cases the dyspnœa should be treated on the lines laid down later. If necessary, hypnotics should be employed. I generally begin with the bromides; or, such mild hypnotics as trional, veronal, medinal, urethane, sulphonal or chloralamide may be tried. Chloralamide acts nearly as well as chloral hydrate in some, though by no means in all, cases, and is supposed to be safer. Paraldehyde is rather stronger; it is an extremely valuable drug in many cases, especially when there is dyspnœa. I have found a drachm of tincture of henbane, in a little hot brandy and water, sometimes succeed where these drugs were not successful. If these remedies fail, chloral hydrate may be tried. This drug has the reputation of being a dangerous remedy in heart diseases, especially in degeneration of the myocardium, but I have used it very extensively and have never found it so. It produces a natural sleep, and is especially useful when nocturnal dyspnœa and supernormal blood pressure are present. It should be avoided, however, where there is much bronchial secretion or œdema of the lungs. It may be given in 5–10 gr. doses by the mouth, gradually increasing to 15 or even 20 gr. if necessary, the dose repeated every two hours, the effects being carefully watched all the time.

If chloral fails, opium or morphia should be resorted to; these drugs are especially useful when there is accompanying restlessness and dyspnœa. The hypodermic administration of morphia is much more efficacious in cardiac failure than when given orally, and there are disadvantages attending the latter method. In regard to dosage, it is well to begin with very small doses, and gradually to increase these until relief is obtained, the effects being carefully watched. Cyanosis is not an absolute contra-indication to the administration of chloral, opium or morphia. Speaking generally, these should not be administered in cases in which there is much bronchial secretion or œdema of the lungs, or in Bright's disease; but in individual cases they may be tried if the first dose is extremely small, and the dosage is subsequently increased with the greatest caution. Further, when there is much bronchial secretion or œdema of the lungs, a sharp look-out should be kept to see if the drug increases this, when atropine or strychnine should be administered in combination with the morphia.

Gastro-intestinal Symptoms.—The treatment of these have been discussed under "diet."

Dyspnœa.—Shortness of breath is often a troublesome symptom, especially at night time. If gastric or intestinal flatulence be present, it should be attended to. Similarly, fluid in the abdomen may require to be withdrawn. If there are indications of congestion or œdema of the lungs, dry cupping should be employed. We should always be careful to exclude hydrothorax as a cause of dyspnœa; when present, paracentesis thoracis should be performed. Diffusible stimulants, such as ammonia and ether, and strychnine may be tried in dyspnœa. Strychnine undoubtedly has an action on the respiratory centre, and in patients who suffer from "night-starts" and nocturnal dyspnœa may be given in full doses in the evening. Venesection or leeching is sometimes of value in dyspnœa. For paroxysmal dyspnœa, vaso-dilators, such as the inhalation of amyl nitrite, or the internal administration of nitroglycerine, erythrol tetranitrate or sodium nitrite, are sometimes efficacious. When these various

measures fail, chloral may be employed, and if this is not successful opium or morphia. The contra-indications to the use of these drugs have already been noted under the head of sleeplessness.

Pain and Palpitation.—The possible causes of pain and palpitation should be carefully considered and adequately treated. Among the causes are gastric and intestinal dyspepsia, especially when attended with flatulence, toxic agents (such as tobacco and tea), hysteria, neurasthenia, anæmia and supernormal blood pressure. The last-named should be regulated by diet, exercise, mercury and saline purgatives, iodide of potassium and the administration of vaso-dilators. Although the effects of vaso-dilators are only temporary they are often serviceable in relieving pain and other symptoms associated with high blood pressure. Among others are amyl nitrite, nitroglycerine, erythrol tetranitrate and sodium nitrite. Iodide of potassium is not infrequently efficacious in cardialgia, even when not associated with supernormal blood pressure. When the pain is obviously due to overstrain or dilatation, rest is especially indicated. The bowels should always be carefully attended to. A belladonna plaster applied to the precordium is sometimes beneficial; while sometimes—especially in acute inflammatory conditions—a mustard leaf, blister, leeching, warm applications, or ice-bag affords relief. If these measures fail the bromides may be given a trial, and in the event of their not being successful it may be necessary to resort to opiates; nepenthe or tincture of opium in doses of 5–10 min. may be tried at first, the amount being subsequently increased as required. If the pain still continues, morphia may become necessary.

Cough.—The cause of the cough, *e. g.* œdema of the lungs or hydrothorax, should be treated. Warm drinks, or a large mustard and linseed poultice over the base of the lungs may be tried. A linctus may be necessary.

Hæmoptysis.—Hæmoptysis is only rarely a serious accompaniment of heart disease. Rest, a dose of calomel and saline purgatives are generally sufficient. A dose of morphia or heroin may be necessary. Venesection or leeching is advocated by some in severe cases.

Pulmonary Œdema.—The special treatment for this is dry cupping, and for acute pulmonary œdema prompt venesection is indicated.

Œdema.—The measures which are of particular value in the treatment of œdema are the restriction of the amount of daily fluid, free purgation, the administration of diuretics, and, in the opinion of many, a salt-free diet. A watery diarrhœa is not necessarily a contra-indication to purgation, because it is frequently due to passive congestion of the intestinal mucous membrane. I prefer a purgative in which some mercurial preparation forms a part, such as calomel and colocynth pill, followed by Epsom salts or some other saline in the morning. Pil. Hydrargyri, 3–5 gr., followed by a saline, may be given once or twice a week for a time. Of diuretics the best are digitalis, squills, caffeine, theobromine, agurin or theocin-sodium acetate, diuretin, scoparium and the acetate, citrate or bitartrate of potassium. With regard to digitalis, the infusion has a greater reputation than any other preparation of that drug in the treatment of dropsy, but I am not sure that this is warranted. Many people prefer a combination of drugs, and, in many cases, this method of treatment often appears to be most efficacious. Baillie's or Guy's pill, which consists of mercury, digitalis and squills, is a well-known combination. It is particularly useful in persistent dropsy due to cardiac failure; indeed, when given along with saline aperients it forms the most useful diuretic in many cases of œdema of heart disease. Among various prescriptions of this combination is the following—

℞ Pilulæ Hydrargyri
Pulveris Digitalis
Pulveris Scillæ
Extracti Hyoscyami aa gr. i
Ft. Pil.

One three times a day after meals.

Another good combination is 5 gr. of citrate of caffeine, 20 gr. of citrate of potash, and ½ oz. of infusion of digitalis.

If digitalis fails, one of the theobromine preparations, such as theocin sodium acetate, or agurin, each three times a day, may be added to it. Diuretin is a very valuable drug.

It is always best, when possible, to give mercury before beginning any of these drugs, as it appears to start the diuresis.

In early dropsy, a flannel bandage wrapped round the limbs is very useful, and this may be combined with massage. When the œdema does not disappear in spite of the measures mentioned, the mechanical removal of fluid should be considered. The means which may be employed are Southey's tubes, acupuncture and scarification. The first two are better than the third. Whatever method is employed strict aseptic precautions should be exercised. The dependent limbs and scrotum may be punctured, and then wrapped in sterilised dressings to drain. If ascites or pleural effusion does not yield to other treatment, and causes embarrassment, the fluid should be withdrawn. With regard to the former, Southey's tubes or tapping may be employed; in the case of the latter, tapping is necessary. When ascites and general ana-

sarca are both present, the one which is the more predominant should be treated first.

Faintness.—Among temporary measures for this complaint are plenty of fresh air, fanning, warmth to the feet, cold to the head and diffusible stimulants, such as ammonia and ether.

Extra-systoles.—Our first duty is to reassure the patient. This may be done with absolute confidence, since there is no evidence for supposing that extra-systoles in themselves—that is, without reference to the conditions with which they may be associated—are indicative either of an impaired heart or add to the gravity of any existing morbid condition. Any associated condition, such as excessive consumption of tea or coffee, or tobacco smoking, gastro-intestinal disturbances, supernormal blood pressure, or neurasthenia, should be treated. The general health should be attended to, and if cardiac failure is present it should be treated on the lines laid down elsewhere. Some hold the opinion that digitalis is of value for the irregularity itself. I have used the drug in many cases, and have never seen beneficial results to follow. The bromides are sometimes of value in modifying or masking the symptoms, especially in nervous subjects.

Tachycardia.—The treatment of tachycardia in heart disease has for the most part been dealt with in the general consideration of cardiac failure. The question of toxic agents (such as tea and tobacco), febrile states, neurasthenia and hysteria as possible causes of tachycardia should always be considered. The bromides, with belladonna, pushed to the limits of tolerance, appear to be of value in some cases of tachycardia.

Paroxysmal Tachycardia.—The results of treatment of this disorder are, in the vast majority of cases, very unsatisfactory. It is true that the paroxysm not infrequently ceases when various remedies are applied; thus, the bringing up of wind, the act of vomiting, the adoption of a certain posture, pressure upon the vagus, friction of the chest wall, and local applications in the form of an ice-bag, mustard leaves, or warmth to the precordia may be followed by relief. But it should be remembered that the nature of the disorder is to stop suddenly even without treatment. During the attack rest is indicated. As far as my observations have gone the remedy which offers most encouragement is strophanthin injected intravenously. The hypodermic injection of digitalin is not so hopeful. Failing the intravenous method, digitalis should be given by the mouth and pushed to the full physiological reaction. If there are indications of heart failure, such as dyspnœa, cyanosis, or dropsy, treatment on the lines laid down elsewhere should be adopted.

Between the attacks, the general condition, and whatever appears to be the exciting cause of the paroxysms, should be attended to. Any gastro-intestinal disorder should always be corrected. Bromides may be tried. In one case—and in one only—in my experience the continuous administration of digitalis proved effective.

Auricular Fibrillation.—In auricular fibrillation, whether there be mitral disease, aortic disease, or disease of the myocardium, if the ventricular rate is rapid, digitalis, or one of its allies, should be administered. The dosage, the choice of preparation, and the question of the great importance of the long-continued administration of the drug in most cases have been fully dealt with.

Auricular Flutter.—The term auricular flutter signifies a morbid condition in which, while the rhythm is normal, the contractions of the auricle are extremely rapid. When the attacks are transient, the treatment is that of paroxysmal tachycardia. When they are of longer duration or the condition has become permanently established, one of the digitalis series of drugs should be administered in large doses, and continued until the pulse-rate has decreased to about the normal, and the distressing symptoms have disappeared. After this, one of two plans may be adopted: (1) the dosage may be lessened, and afterwards the administration of the smallest dose necessary to control the ventricular rate continued in the hope that the flutter may cease; and (2) large doses may be continued, in the hope of inducing auricular fibrillation, after which the administration of the drug is discontinued for some days, in the hope of a return to the normal rhythm.

Bradycardia. Partial and Complete Heart-block. Adams-Stokes' Syndrome.—The cause of bradycardia should be attended to. When heart-block occurs during the course of infective diseases, rest in bed is indicated, and the cause, such as rheumatism, should be adequately treated. Persistent heart-block of mild degree requires no treatment in itself. But, as there is usually valvular or myocardial disease or both, it is of great importance that the patient should live strictly within the limits of the heart's strength. This is of still greater importance in cases of persistent heart-block of severe degree. Accordingly, the daily life of the patient should be most carefully regulated, and undue physical or mental strain should be scrupulously avoided. When there is reason to suspect that syphilis is the cause, appropriate and energetic anti-syphilitic treatment should be employed. When heart-block is associated with arterio-sclerosis, the amount of food, alcohol and exercise should be regulated, iodide of potassium should be tried, and if the blood pressure is high it should be regulated. If the patient is subject to fits, he should

be warned to avoid anything known to predispose to the attacks, and as far as possible he should be protected from the risks of falling. Unfortunately there is no drug which undoubtedly accelerates the ventricular rate of contraction, and, therefore, none is efficacious during an attack. Digitalis may be tried in cases of complete heart-block in which there is dropsy or some other indication for its use, for the drug does not slow the ventricle when that chamber is contracting independently of the auricle. Atropine may be given a trial, since cases of Adams-Stokes' syndrome have been recorded in which the writers have stated that, in their opinion, the drug was the means of increasing the pulse-rate and giving relief to the symptoms. $\frac{1}{100}$ gr. may be given hypodermically, and repeated in half an hour if necessary. I myself have never seen any good result follow its administration in this disease. Strychnine, oxygen and amyl nitrite have been administered, but there is no reason to suppose that they are of any value.

Pulsus Alternans.—As pulsus alternans is a sign of very great exhaustion of the heart muscle, complete and long-continued rest, both physical and mental, is urgently needed.

Supernormal Blood Pressure.—When supernormal blood pressure is present, attempts should be made to regulate it by the methods described in the article on *Diseases of the Arteries.*

B. Methods of Treatment Applicable to Individual Cardiac Affections

It should be clearly understood that the measures described as applicable to any cardiac affection in the main hold good in regard to individual cardiac affections. If this be taken for granted, much needless repetition will be saved in describing the treatment of individual disorders. The importance of rest whenever there are any indications of cardiac failure, the indications for, and the methods of, administering the digitalis series of drugs and other measures, as well as the treatment of symptoms, have already been fully described.

Acute Simple Endocarditis and Acute Myocarditis.—The management of a case of acute simple endocarditis or of acute myocarditis is of great importance, especially in regard to the future life of the patient. Acute rheumatism is by far the commonest cause, and it should be remembered that it is easy to overlook a rheumatic infection of the heart in childhood, since rheumatism in children presents many and important differences from the disease as it appears in adult life. In childhood articular inflammation is usually slight, and may even be entirely absent; while endocarditis and pericarditis are much more frequent, and should not be looked upon as complications but just as much part of the disease as is the affection of the joints. Subcutaneous nodules, the exudative erythemata, and purpura rheumatica are also more frequent manifestations of the rheumatic infection; while chorea also is common in connection with the rheumatism of childhood. While endocarditis may occur acutely in children as it does in adults, it more often occurs in a subacute and insidious form, and therefore its existence is frequently not known or suspected until the heart is examined.

When any child complains of pain in the joints, muscles, or tendinous structures, or of what are called "growing" pains; or has subcutaneous nodules on the tendons or round the joints, or subperiosteal nodules on the bones; or exhibits an erythematous eruption; or if there is a suspicion of chorea; or suffers from malaise and unexplained pyrexia; or complains of pain in the chest or shortness of breath; or presents marked pallor; he should be at once put to bed, and the heart examined carefully and systematically every day. Otherwise, a large proportion of the cases in which cardiac mischief occurs will be missed altogether.

When there is no doubt that the heart is affected by rheumatism, the indications for treatment are definite.

In the opinion of some, salicylates should be avoided when there is undoubted cardiac involvement, in the belief that when given for considerable periods they depress the heart and cause further dilatation. I do not share this view. Some prefer iodides to salicylates, given in full doses over considerable periods. A vaccine of the diplococcus of rheumatism is recommended by some, while cases have been recorded in which the administration of antistreptococcus serum, particularly in the prolonged or recurring cases, has apparently been attended by beneficial results. It may be given in 10 c.c. doses subcutaneously once a day for a week.

When the cause is other than rheumatism, it should be treated on the lines laid down elsewhere.

In all cases, whatever the cause, in which there is acute endocarditis or myocarditis, absolute rest in bed is indispensable. Its object is to assist the process of repair. At no stage in the management of a case should the heart be allowed to work up to the limit of its capacity. In the majority of cases absolute rest in bed is necessary for three months, and in some cases the period should be even longer. The patient should remain in the recumbent posture for at least a month after the fever has subsided. If tachycardia, or irregularity indicative of partial heart-block or of auricular

fibrillation, or if pulsus alternans be present, this period should be longer, even to three or four months. During the period that the patient is in the recumbent posture, he should on no account be allowed to sit upright in bed or to get out of bed for an action of the bowels. Afterwards, the amount of exertion should be most carefully graduated. At first, an extra pillow may be allowed. A few days later, the back may be slightly raised, and this may be gradually increased until the patient is moved on to a couch, in which position he should continue for a further period of three months. After the first two or three weeks of this period, very gentle massage may be allowed; and during the latter six weeks the massage may be increased, active movements may be indulged in, and the patient may be gradually allowed to sit up. Later, slight walking exercise may be permitted. For some months later great care should be exercised with regard to exertion, and the patient should be given rules as to the amount and kind of exercise; for, on the one hand, exercise may do much harm unless carefully regulated, while on the other hand it is of great value in moderation. If, during any of these stages, exertion is accompanied or followed by undue breathlessness, palpitation, sense of fatigue, precordial pain or distress, or increased frequency of pulse, the patient is doing too much and the amount of exertion should be reduced. Excitement and worry of every kind should be avoided. The diet should be light, small in bulk, yet highly nutritious and preferably solid. The daily amount of fluid taken by the mouth should be restricted to two pints of fluid per day. Saline infusions per rectum, or in grave cases intravenously, may be added. Strict attention should be paid to the bowels, preferably by mercury and salines.

In acute endocarditis, the internal administration of iodide of sodium in the later stages is employed by some. Dr. Caton recommended small blisters applied repeatedly to the precordium; I myself have been disappointed with the results. Mustard leaves may be used instead. Alcohol should not be given unless there is much exhaustion, dyspnœa, cyanosis, or an unduly rapid pulse. In these cases oxygen may also be employed. Alcohol is believed to be of particular value in the cardiac failure due to acute myocarditis. The best forms are good old brandy and champagne. The amount required of course varies with each individual case. It is well to begin with 2–3 oz. per diem, gradually increasing the quantity as required. For an ordinary severe case I generally average 6–8 oz. of brandy in the twenty-four hours. I never go beyond 10 oz. per diem. The amount should be gradually decreased as the patient improves. Other diffusible stimulants, such as ether and ammonia, may be employed. Camphor and tincture of musk are used a good deal on the Continent of Europe. Strychnine has a great reputation in the treatment of cardiac failure due to acute myocarditis. It may be tried when there is great exhaustion. In the writer's opinion, it is much better given hypodermically. In severe cases it may be given up to $\frac{1}{60}$ gr., or even $\frac{1}{30}$ gr., every two hours. The results of the administration of the digitalis series of drugs are, as a rule, extremely disappointing. The response is usually very slight, if at all, whether auricular fibrillation is present or not. In suitable circumstances quinine may be administered; and if anæmia is present iron and arsenic may be prescribed. When the blood pressure is very low, 5 min. of a 1 in 1000 solution of suprarenal extract, or pituitary (infundibular) extract, may be administered by the mouth. The treatment of symptoms has, in the main, been dealt with previously.

For precordial pain or distress, a hot linseed poultice may be applied to the precordium, and if this fails the continuous application of an ice-bag may be tried. Dover's powder (10–15 gr.), or, if necessary, morphia may be given by the mouth. In the less acute pain a fly blister is not infrequently efficacious. During convalescence extreme care should be taken not to allow the patient to do too much.

Malignant Endocarditis. — Needless to say, absolute rest in bed is *the first* essential, and exposure to the open air is of value. The teeth should be carefully attended to; if pyorrhœa alveolaris is present, it should be treated. The diet should be fluid and liberal in amount, and the bowels carefully regulated. Many drugs have been employed in the treatment of this disease, among them being quinine, the sulphocarbolates, carbolic acid, mercury, arsenic, formalin, and the organic preparations of silver (such as protargol). Quinine is probably of value in lowering the temperature. In those cases in which leucocytosis is absent or slight, nuclein may be given by the mouth, subcutaneously, or even intravenously. If given subcutaneously the dose should be 5–15 min. of a 10 per cent. solution once a day. Silver salts may be given in combination with nuclein.

Within recent years specific measures, in the form of vaccines and antisera, have been extensively employed in the treatment of this disease, but the results, on the whole, have not been encouraging. Some combine the two methods. Better results are obtained from the patient's own micro-organisms than from stock vaccines. An attempt should be made to isolate any organism which may be present in the blood, and if successful a vaccine should be

prepared. The question of dosage and the determination of the proper intervals between successive doses is difficult. Formerly it was thought that frequent estimations of the opsonic index afforded a good guide. We now know that this is not the case, if for no other reason than the fact that in malignant endocarditis there is a constant fluctuation of the index. The clinical symptoms and temperature, however, are of service, and should be carefully noted. It is most important to avoid too large and too frequent dosage. We should begin with a small dose, and proceed very cautiously, both in regard to an increase of dose and in lessening intervals between the doses. If any dose is followed by pain in the limbs, headache, increase in the severity of symptoms, or rise of temperature, it is either too large or the period of time that has elapsed since the preceding dose has not been sufficiently long. In such a contingency, the next dose, therefore, should be a smaller one (perhaps a half or even less), and it should not be increased for some little time, and, as a rule, at a longer interval. As an example of dosage and spacing of the doses, we may try 2–5 millions streptococci or 50–100 millions staphylococci to begin with, administering a second dose after an interval of 3–5 days, and carefully watching the effects. During the time that the vaccine is being prepared from the patient's own micro-organism a stock preparation of the micro-organism may be employed. When streptococci are found, anti-streptococcus serum (univalent or polyvalent) may be employed. Ten c.c. may be given subcutaneously, or 15 c.c., per rectum, daily for three or four days, after which there should be an interval of several days. If the administration is followed by an increase of symptoms or rise of temperature, small doses, such as $2\frac{1}{2}$ c.c., should be substituted. When the condition is due to the pneumococcus, Merck's or Pane's antipneumococcus serum may be tried in full doses.

The daily administration of normal horse serum, either subcutaneously or intravenously, has recently been well spoken of.

In cases with an unduly rapid pulse, great exhaustion and cardiac dilatation, alcoholic stimulants and strychnine may be employed. The best method of reducing the temperature is tepid sponging of the body; of drugs, the best is quinine. Other symptoms should be treated on the lines laid down elsewhere.

Hypertrophy.—This in itself does not need treatment. It is always advisable, however, to consider the cause, and, in some cases, as for example, when chronic Bright's disease, supernormal blood pressure, or arterio-sclerosis is present, it should be suitably treated. In order to provide a good supply of food to the heart muscle, we should see that the patient gets plenty of fresh air and an adequate supply of nutritious and easily digestible food, and if dyspepsia or anæmia is present it should be attended to. Undue physical or mental strain should be avoided. If cardiac failure supervenes, it should be treated as described elsewhere.

Dilatation. Mitral Insufficiency apart from Structural Alteration of the Value.—Dilatation of the left ventricle apart from structural alteration of the value may cause mitral insufficiency. The cause, such as chronic Bright's disease, supernormal blood pressure, arterio-sclerosis, aortic disease, undue physical strain, alcoholism, bacterial poisoning, influenza or anæmia, should be attended to. Rest is imperative. Other general measures, as well as special forms of treatment, and the treatment of symptoms have been described. If auricular fibrillation is present, in association with a rapid pulse, digitalis is clearly indicated. When the dilatation is due to poisoning, digitalis appears to be unavailing.

Chronic Myocarditis. Myocardial Degeneration.—In either condition it is of great importance that the patient should curtail his physical and mental activities so as not in any way to exceed the limited strength of the heart. The daily life of the patient should be gone into with great care and in detail. Carefully regulated exercise in the fresh air is useful, but violent and sudden efforts should be strictly forbidden. Scrupulous care, however, is necessary in this direction. The amount and kind of exertion should be adapted to each individual according to the strength of the heart muscle. Such exercise as walking against a wind, and cycling uphill are contra-indicated; on the other hand, quiet walking on the level, or even slow walking up an incline, quiet cycling, croquet, and even riding or golf may usually be allowed, excepting in advanced cases. Exertion should stop short of producing undue breathlessness, palpitation or fatigue, a sense of tightness across the chest, or precordial pain or distress. If these precautions are not taken there is real danger. Even when there are no indications of cardiac failure, periods of complete rest are often useful. High altitudes are better avoided. Only warm bathing should be allowed. The clothing should be warm. Particular care should be taken in regard to diet; it should be most carefully regulated on the lines previously laid down.

Gastric and intestinal dyspepsia, especially with flatulence, should be avoided, or treated when present. What fluid is taken with meals should be taken *at the end of* meals. Overloading of the stomach should be avoided. Rest before and after food, and in the after-

noon, should be enjoined. The state of the bowels should be carefully attended to. In these cases, it is sometimes of advantage to diminish the body weight. If there is supernormal blood pressure it should be regulated by the methods described elsewhere. If anæmia is the cause or an accompaniment of the condition, it should be adequately treated.

When there are indications of cardiac failure, rest, proportionate to the degree of failure present, is imperative; other therapeutic measures, also, as previously described, should be adopted. The indications for one of the digitalis series of drugs have already been pointed out. Even in cases of auricular fibrillation in association with a rapid pulse, as a rule the response is not so good as in heart disease following rheumatism. Such complications as angina pectoris may require to be treated.

Fatty Infiltration.—Treatment consists mainly in dieting, systematic elimination and abundance of fresh air, while carefully regulated exercise and other measures which have for their object the reduction of bodily fat should also be employed. The diet should be strictly moderate in amount, and sugars and starches, especially bread and root vegetables, should be proportionally diminished; the diet, therefore, must be mainly nitrogenous. The food should be eaten slowly and thoroughly masticated. The amount of fluid with meals should be restricted, and what is taken should be taken at the end of the meal, while, on the other hand, a considerable quantity of fluid between meals is advisable. It is better to avoid alcohol altogether, but, if this is not possible, brandy or whisky, well diluted, Moselle, or claret are much preferable to malt liquors, Burgundy, port and champagne.

Regulated exercise in the open air, such as walking, riding, golfing and cycling, are valuable. Exercise indoors, as, for example, the use of dumb-bells, is of benefit as adjuncts. Graduated exercises are of special value in cases of slight failure due to fatty infiltration. In my opinion the simple forms of movements are, certainly in the majority of cases, better than the resistance exercises practised at Nauheim. These movements may be indulged in even when the patient is confined to bed. With regard to all forms of exertion, care should be taken that it is at first limited in amount and only gradually increased, while it should stop short of producing any indications of cardiac distress. Systematic elimination by means of purgatives, Turkish baths, and a visit to a spa, such as Harrogate, is sometimes useful.

Valvular Disease.—If there are no indications of cardiac failure no direct treatment is necessary. But explicit and detailed instructions in regard to the manner of life he should lead (as fully described under general measures) should invariably be given to the patient. The importance of always living within the limits of the heart's strength and the avoidance of sudden and violent effort is of especial importance in aortic disease. The teeth, gums and bowels should invariably be attended to, in order to diminish the risk of malignant endocarditis. In mitral disease due to structural disease of the valve, the patient is liable to attacks of bronchitis and bronchopneumonia; while in both mitral and aortic disease in children and young adults there is the liability to subacute and acute rheumatic attacks. Preventive measures in regard to these should be adopted. When, in valvular disease, there are indications of cardiac failure, such as dyspnœa, it is imperative that the work of the heart should be lessened by rest. If the cardiac failure is slight in degree, continuous rest in bed is often not necessary; it is often advisable, however, to begin treatment by keeping the patient in bed for a little time. Other measures which may be adopted, as well as the indications for the administration of digitalis, have been dealt with already. In mitral disease the tendency is for the occurrence of cardiac failure, while in aortic disease the patient is especially liable to pain in the precordium and to cerebral symptoms. The treatment of these has already been described.

Congenital Heart Disease. — The general measures previously laid down are applicable also to this affection. It is particularly important that the child should be kept warm, and it is imperative that careful and detailed measures should be adopted for the prevention of bronchitis. When cardiac failure supervenes, it should be treated on the lines previously described.

Angina Pectoris. — The treatment of true angina pectoris resolves itself into two parts: (1) that which aims at preventing the recurrence of the paroxysm; and (2) that which has the object of relieving the paroxysm.

With regard to the first of these, we should try to improve the general health, more especially the circulatory and nervous system; and since the condition occurs usually in association with exhaustion of the heart muscles, a cardinal indication is to try and remedy this exhaustion and to prevent its recurrence. In this connection, it is advisable first of all to review the etiology of angina pectoris, and to endeavour to find out the cause of this exhaustion, and for this purpose it may be necessary to inquire in detail into the past and present life of the patient. In some cases the clear indication is to enjoin rest, proportionate to the degree of exhaustion. With this object in view, it may be necessary to order complete

rest in bed for some time, and even to give sedatives, such as chloral or opium. Morphine is in most of these cases more useful than opium itself. After a period of rest explicit instructions should be given to the patient that in future he should live within the limits of the heart's strength. He should avoid any exertion which produces undue breathlessness, palpitation, or fatigue, as well as hurry, sudden effort, walking or hurrying against a cold wind, especially after a meal. Cold sheets at night should also be avoided, and a cold bath in the morning should be prohibited. The nervous system may be a factor in the production of angina pectoris, and when there is reason to believe that this is the case appropriate measures should be employed. When the patient has suffered from a period of mental strain or sleeplessness, and, indeed, whenever there is any excitability or irritability of the nervous system, the administration of bromide of ammonium, in doses of 10–20 gr. three times a day is often of great value. Emotional excitement, gastro-intestinal dyspepsia—particularly that form which is accompanied by flatulent distension—constipation, and all other possible exciting causes of the attacks should be carefully avoided or treated when present. Over-indulgence in diet, alcohol and tobacco should be avoided. Flannel should be worn next to the skin both summer and winter. When there is reason to believe that syphilis is the cause, appropriate and energetic anti-syphilitic treatment should be employed. Similarly, if high tension is present this should be treated on the lines laid down elsewhere. Indeed, we should review the whole of the causes of angina pectoris, predisposing and exciting, with a view to treatment. Of drugs which may be given with the hope of preventing an attack, the most hopeful are iodide of potassium and nitroglycerine. The former is probably in most respects the best, and is particularly indicated when arteriosclerosis is present, more especially if there is a history of syphilis. In some cases 5 gr. doses are sufficient, while in others the drug should be pushed. Nitroglycerine may be given in the form of tablets or the pharmacopœial solution; one-hundredth of a grain be given three or four times a day, and gradually increased to $\frac{1}{20}$ gr. or even $\frac{1}{10}$ gr. Either drug should be given intermittently for two or three weeks at a time, while in some cases it is good to alternate them. Sodium nitrite, erythrol tetranitrate, mannitol nitrate and nitrite of potash are other drugs which may be employed. Taken altogether, the nitrites are not so valuable as the iodides.

For the paroxysm, the most efficacious remedy in most cases is the inhalation of nitrite of amyl; the action of the drug is almost immediate and the relief is usually complete, this being particularly so in cases of widespread arterial constriction. In many cases, however, it is absolutely useless. It is best administered in the form of the glass capsules or perles, which the patient should carry about with him. Each contains from 3 to 5 min., and one should be crushed between the folds of a handkerchief and inhaled freely. The dose may have to be repeated. A similar effect may be obtained by nitroglycerine, but its action is not so rapid, while its effect is more prolonged. It may be given in the 1 per cent. solution of trinitrin, beginning with 1 and increasing if necessary to 5 min. doses, in a little water; or, the patient may nibble one or more tablets until the pain disappears. If there be flatulent distension, a draught of carminative mixture, or if this be not available some very hot water with a little essence of peppermint or brandy, sipped slowly, may be given with the amyl inhalation or the nitroglycerine drops. In cases in which there is pronounced heart failure, brandy or ether, preferably the latter, in doses of 20–60 min., in which 1–2 min. of trinitrin (1 per cent. solution) may be dissolved, may be injected subcutaneously. Erythrol tetranitrate and sodium nitrite are not so suitable for these attacks. If the drugs enumerated fail, chloral by the mouth, hypodermic injections of morphia, or inhalations of chloroform should be employed. Twenty grains of chloral hydrate may be tried. As a rule it is necessary to give morphia in larger doses ($\frac{1}{4}-\frac{1}{3}$ gr.) than in other disorders. A $\frac{1}{50}$ gr. of nitroglycerine may be combined with the morphine. The nitrites and chloroform are not of such value in cases in which there is an absence of decided arterial spasm as in cases in which it is present. Where there is cyanosis or asthma, oxygen inhalations may be tried, particularly in those cases in which morphia is found necessary. If the drugs enumerated are not at hand, hot drinks, water containing whisky, or brandy, capsicum, spirits of chloroform, or a carminative mixture, may do good by the relief of flatulence.

F. W. P.

ATHLETIC OVERSTRAIN OF THE HEART

Overwork of the heart in an athletic boy usually first affects the left side; and in an athletic young man, the right side. The features of the attack vary with the part involved and the degree of overwork; when the right side is concerned, the earliest stage is a tumultuous state of inefficiency, while the same stage of a left-sided case is an intermittent disturbance passing off with exercise and reappearing with rest. Loss of tone is marked in both cases. To mention some of the features:

breathlessness, shallow respirations, deep coloration of the face, aching and "tightness" of the chest, increased pulse frequency *in all positions* and high blood pressure irrespective of posture point to right-sided trouble. Later there may be a diffuse, "wavy" impulse and epigastric pulsation. On the other hand, a sense of great insecurity, with loss of power, nausea, chilliness, breathlessness *on exertion*, fall of blood pressure and of pulse-rate to a subnormal level on resting, and a leaden hue point to the left side. When both sides are affected there still remains the stamp of one side or the other with fresh features, *e. g.* tenderness, especially of the "apex," spacing of the heart sounds amounting at times to something very like a tic-tac rhythm with a rise in pitch and a fall in volume, loss of tone which persists for weeks instead of for days, crepidations at the base, more often of the right side. The heart has no power of adapting itself to either work or position until the pressure is lowered. This degree of overwork is not reached *suddenly* in a healthy athlete.

The degree of enlargement is of no great use as evidence of overwork for two reasons. We do not know the size of the heart due to hypertrophy in any particular case, and the increase in size may be apparently no greater than that seen in the same heart at the end of an ordinary day which has included some very vigorous exercise.

The ability to take hard exercise rapidly decreases in athletic boys and men *who have allowed themselves to become soft*. They are apt to forget this and suddenly determine to go to the help of a team in a "tight place" with very evil results to themselves at times. In extreme cases their symptoms and signs are: blueness, breathlessness, a running pulse with rapping heart sounds, dilatation of the auricle which can be percussed out, engorgement of the veins. Percussion of the ventricle at this stage shows little or nothing because of the jerky breathing with distension of the chest.

At a later time one can satisfy oneself that the cardiac dullness is increased over the ventricle much more than it ever seems to be in the healthy athlete, however overworked his heart may be. (Acute dilatation in a *healthy* young athlete of the whole heart has never come my way; possibly I have missed it. Such a patient's margin of safety is stupendous.) All degrees of this are seen between one extreme marked by breathlessness and perhaps an occasional thud of the heart with passing increase of breathlessness and the other rarer extreme just described. The most troublesome result to the patient is irritability of the heart not by any means purely psychical. It is a real inefficiency, with a definitely greater and widespread consciousness of the beats of the heart, regular and irregular. The consciousness can be favourably influenced by valerian and the mixed bromides of sodium and ammonium, and he sleeps better, but there remains difficulty in regaining the reserve power of the muscle. I do not desire to be dogmatic, so I give my evidence, which is this: I have seen over 300 irritable hearts in fifteen years, not all of home manufacture, and not one of them has got better while the patient was allowed to take exercise, which, while in health, he would have looked on as trivial. The most important factor in treatment is rest, and *enough of it*. The patient must be put to bed, and if there is a high blood pressure it should be reduced; for this purpose diuretin 15 gr. every two or three hours is sufficient and does not depress the heart. The first sign of recovery is that the circulatory system "breaks away" from the influence of the drug as shown by a rise in pressure and in pulse frequency.

When there is no longer increasing pulse frequency I have generally found the heart fit for carefully graduated passive exercises, progressing to sitting up in bed and so on. This usually occurs after three days of rest in a right-side affection. Any sign of irritability or weariness, such as extra systoles or the dropping of a beat, followed by a thud or a succession of weak beats is an indication that the work of the heart should be lessened again.

Another method which is often beneficial is the full-length hot bath. The room should be well ventilated and the patient kept in the bath at as high a temperature as he can stand till he begins to sweat. He should then be *lifted* out and *carried* to a *warm* bed. The room should be darkened and sleep promoted by a draught containing, *e. g.* chloral hydrate 10–20 gr., sodium bromide 10 gr., and ammon. bromide 10 gr. After a sleep the patient may wake up quite comfortable and may have no return of symptoms. This treatment is specially suitable for patients who are keenly sensible of a "bumping" of the heart. As the blood pressure falls the other symptoms tend to subside gradually. The after-treatment of these right-sided cases involves careful restriction of food and exercise so that there is no risk of cardiac overwork for a period of three months. Cause: Often deficient chest movement.

When the left side is affected, rest in bed is also necessary. Pulse-rate and blood pressure then fall below normal, sometimes in one or two hours. In one such case I observed a pulse-rate of 39 and a blood pressure of 90 mm. (Riva-Rocci). On attempting to sit up the pulse-rate increased to 130, while the blood pressure only rose to 110 mm. The most useful drug at this stage seems to be strophanthus. While waiting for it to act a

diffusible stimulant should be at hand in case of respiratory discomfort which may come on when the patient is first put at rest. These hearts respond more readily to drugs of the digitalis series than do diseased hearts. Strophanthus is well borne by the stomach, but digitalis should be substituted as soon as the heart begins to settle down to a more regular rhythm, and the risk of vomiting is past. It produces its finest effects when given regularly day after day in as large doses as can be taken without exciting nausea or subjective consciousness of the heart's action. Reduction in the amount taken should be brought about by reducing the number of successive days in the week on which the drug is given, and not by reducing the dose or the number of doses a day. *Gradated* exercise should be resumed as soon as the heart has steadied. The earliest forms of exercise should be gone through while *lying* on the bed, the latest on a level road escorted by a vehicle. The test of the heart's condition is its increase in speed of beat: when this is more than 10 to 15 per cent. two minutes after coming to rest in a sitting position, it is being asked to do too much. I am assuming that the blood pressure does not fall when the heart quickens, if it does the state of affairs is not merely overwork. To allow of complete recovery very gradual increase of exercise, abstention from tobacco and from all stimulating foods, avoidance of all forms of excitement, and in some cases even of any forms of *keen* interest are necessary.

The need for immediate treatment in the severe degree of overwork and enfeeblement seen in the unfit is met by venesection and the withdrawal of 15 oz. of blood coupled with the use of a vaso-dilator to prevent any subsequent rise of blood pressure. When walking on the level begins, a wary eye must be kept on the pulse at the time of exercise, and until the patient can walk a mile without persistent quickening of the pulse, every walk should end where his doctor can see him.

In this way much irritability and its attendant limitation of usefulness, as well as the enlarged inefficient heart which is only good for a regular procession of easy days, are avoided.

These patients are helped by anything which improves the condition of the blood, *e. g.* arsenic and iron, the former drug being of the greater importance; hæmoglobin and glycerophosphate of manganese; digitalis later on in full doses. When digitalis is followed by doubling of the beat or quickening of the rate of single beats I have been accustomed to replace it by tincture of cactus grandiflorus in doses worked up to 30 min. (or by cactina pellets—lately I have not used these); it carries the heart on until digitalis can be resumed in full doses without untoward effect. I have read that it is useless, but coloured water allows the heart to relapse while still liable to the unwished-for influence of digitalis.

R. W. M.

DISEASES OF THE ARTERIES AND ANEURYSM

The physiological function of the arteries is to convey to the various parts of the body the blood pumped into them by the heart. They are not mere mechanical tubes, but have elastic living walls whose healthy condition is of the greatest importance both for local and general circulation. The compelling pressure under which the blood flows is derived originally from the force of the heart-beat, and the intermittent pulsation in the arteries is converted into a regular flow in the capillaries by the elastic arterial walls and the resistance offered by the small arteries to the escape of blood through them. This resistance varies inversely as the calibre of the arterial tube, and therefore depends on the active muscular contraction or tone of the vessel walls. Arterial tone is itself dependent on the central nervous system through the vasomotor nerves and the vasomotor centres in the spinal medulla and medulla oblongata.

Therapeutically it may be advantageous to diminish or increase the quantity of blood flowing through a particular organ or part of the body, or to raise or lower the general blood pressure.

Alterations of Local Blood Flow.—The amount of blood arriving in a particular portion of the body can be decreased by making the afferent vessel smaller, provided no alteration is produced in the rest of the vascular area. This may be accomplished by direct compression, or by causing a reflex contraction of the vessel wall by means of cold applications. The supply of blood may also be diminished by making use of gravity, *e. g.* raising a limb above the level of the trunk decreases its supply owing to the difficulty of flow against gravity. So far no drugs are known which have a selective constricting action on particular vessels apart from a general effect on all the arteries.

The local supply of arterial blood may, on the other hand, be increased by placing a limb in a dependent position, or by causing a dilatation of the afferent vessel as by the application of warmth. A useful method of flushing a limb with arterial blood consists in first emptying it by the application of a Martin's rubber bandage: after the removal of this there is a temporary loss of arterial tone, with the result that a very large amount of blood flows into the limb, giving it a bright red colour. Massage,

besides pressing out the venous blood, leads to arterial dilatation, and so materially augments the flow through the part treated. Certain drugs have the reputation of bringing about local arterial dilatation; for instance, pilocarpine acts in this way on the arteries of the skin and the salivary glands. Digitalis is supposed to cause a special dilatation of the renal arteries, while constricting all the others: the exact mechanism by which digitalis works on the human system is still somewhat obscure, but diuresis is often produced apart from any effect on the heart.

The General Arterial Pressure, on the other hand, varies inversely as the size of the vessels, thus a general dilatation of the arteries brings about a fall of pressure, while constriction causes a rise provided the force with which the blood is pumped out of the heart remains the same. The arteries, and here the most important are the small ones, dilate under the influence of warmth (*e. g.* a hot bath), with exercise or massage, and with the administration of certain drugs. Exertion raises the pressure while it continues owing to increased vigour of the heart-beat and compression of the vessels by the muscular contraction, but this is followed by a fall that lasts longer than the original rise. Of course a fall of arterial pressure, provided it is not due to extreme feebleness of the contractions of the heart, leads to an increase of pressure in the capillaries and veins, and of the latter the large veins in the splanchnic area require special mention since they can contain the whole blood in the body. The arterial pressure can naturally be raised by pressing the blood out of these veins, as, for instance, by applying a tight bandage to the abdomen. On the other hand, a sudden diminution of external pressure here may lead to a dangerous fall of arterial tension, the patient bleeding, as it is said, into his abdominal veins.

When one comes to the treatment of an individual patient it has first to be considered whether his blood pressure is to be regarded as abnormally high or low. It is impossible to fix a standard of high or low pressure, and it must not be forgotten that the pressure gradually increases with age, so that what may be abnormally high in the young becomes quite normal in the middle-aged. Then, again, excitement, exertion or tobacco-smoking may cause a temporary rise of pressure, which as recorded by an instrument may mislead the observer. As a rule the physician has to deal with cases of abnormally high tension in persons over the age of forty, and in these a permanent maximum pressure of over 160 mm. of Hg. should be regarded with suspicion. It is important to recognise that sometimes the maximum pressure is decidedly raised without any increase in the minimum pressure, so that the mean is but little raised: these cases have not the same serious outlook as those where there is decided elevation of the mean pressure. Cases of high arterial pressure, especially where there is also disease of the arterial wall, are prone to paroxysmal attacks of further raising of the pressure which may last several hours. On the other side maximum pressures that do not reach 90 mm. of Hg. should be regarded as suspiciously low and as possibly in need of treatment.

Treatment of High Arterial Pressure.—Having decided that the pressure in a particular patient is abnormally high the physician has next to determine whether it is advisable to attempt to reduce it. In many persons a high pressure is compensatory and an efficient capillary circulation cannot be maintained without it. Here, obviously, it is inadvisable to spoil the proper working of the machine by trying to make one of its parts fit in with some arbitrary standard. Other persons feel all the better when the pressure is high, and unless there is urgent need for lowering it they should not be treated. The raised tension may occur in persons whose vessels are in themselves healthy, or in others where the arterial walls are already degenerate. There is a good deal of evidence that constant increased arterial pressure is one of the commonest causes of arterial degeneration, so that it is important to start treatment as early as possible, recognising that in no condition is the old adage that prevention is better than cure more apposite.

One finds that both arterial disease and increased arterial pressure are commonest in persons leading a sedentary life, whose labour is mental and whose recreations include a free indulgence in both eating and drinking, with elaborate cooking and a good deal of alcohol. There is, therefore, justification for the view that these are potent causes of the pathological abnormality, and the first essential of treatment is to remove the causes of disease. In the vast majority of cases, all that is necessary or advisable is to see that the patient does not work his bodily mechanism at too high a pressure. He should be relieved of some of the cares and excitement of business, his diet should be less ample, and the cooking less elaborate, and he should get regular moderate exercise in the open air in the form of riding, walking or golf. The consumption of alcohol should also be restricted and carefully regulated. In prescribing such a régime, it is important to avoid regarding the patient as in any way an invalid, since high arterial pressure is tending to become one of the favourite hypochondriacal fads of later middle age, but some such measures are required in all cases of decided high arterial tension.

Where the raised pressure is persistent, or where there are already signs of arterial de-

generation, further treatment may be necessary. The intake of salt and extractives should first be lessened. Thus soups must be forbidden, and meat should usually be boiled, as in this way the extractives are removed. Next, a still greater restriction of diet, especially with regard to the proteins, should be ordered, and an attempt made to lower the pressure further by the use of drugs, particularly those that cause a dilatation of the peripheral arteries. Unfortunately in these cases, an artificial reduction of tension is usually followed on cessation of treatment by a return to the original high level, while many patients are prone to paroxysms of high pressure lasting several days, and the passing away of such a paroxysm may unduly flatter the therapeutic measures.

The drugs with the most decided influence on the reduction of pressure are the nitrites. Some of these, such as amyl nitrite and nitroglycerine, have a rapid and considerable effect, which, however, only lasts a very short time, whereas the nitrites of sodium and erythrol act more slowly and less energetically, but produce a more prolonged result. The former are, therefore, more suitable where a rapid temporary decrease of pressure is desirable, *e. g.* in angina pectoris, and the latter are more adapted for continued administration where a more permanent effect is hoped for. Of other drugs, the benzoates and hippurates (*e. g.* 1–2 gr. of ammonium hippurate two or three times a day) are strongly recommended by Oliver, and these may be combined with nitrites. Oliver also advocates the combination of alkalies, with vaso-dilator drugs. Iodine in the form of potassium iodide has long held a reputation in the treatment of this class of case. Although it is impossible to demonstrate any direct effect in the reduction of tension, there is no doubt that the patients, particularly where there is some arteriosclerosis, feel benefit from the course of the drug, of which 3–5 gr. should be given three times a day over several months.

In renal disease, or in patients in whom cerebral hæmorrhage is threatening, the physician may feel it incumbent to produce a rapid and material reduction of pressure. Here bleeding is of great service, and it is in this class of patient that we so often see a marked improvement in the general condition after a smart epistaxis. Sweating, by means either of the hot-air bath or the hypodermic administration of pilocarpine, also assists in lowering the arterial tension and relieving the symptoms of the patient. In all cases of high arterial pressure it is important to see that the bowels are acting well and regularly, since it is possible that the original cause of the rise of pressure is some toxin of intestinal origin. Where the pressure is excessively high, a maximum of over 200 mm. of Hg., free purgation seems to assist in the reduction.

Treatment of abnormally low arterial pressure is but seldom required, except as an urgent condition due to shock, feeble cardiac contractions, etc. The necessity is adequately met by temporary measures which stimulate the contraction of the heart, cause a constriction of the peripheral arterioles or forcibly drive blood out of the abdominal veins. Thus the heart contraction may be stimulated by alcohol, ether, ammonia or strychnine, or even by direct irritation; the arterioles may be caused to contract by the administration of suprarenal or pituitary extract, which probably also stimulate the cardiac muscle: and the abdominal veins may be emptied by direct pressure, such as exerted by a firm bandage applied to the abdomen. It is remarkable that the blood pressure is not usually materially lowered in the condition to which the clinical term "heart failure" is applied, where there is general venous congestion and dropsy, except when the condition is extreme and death impending. Should the pressure be low any measure that results in improved action of the heart would tend to raise it to the normal level, so that free bleeding and the employment of such drugs as digitalis would incidentally improve the blood pressure.

Some persons enjoy good health even in spite of a constant pressure below the normal. Neither in these cases, nor where a low pressure is associated with chronic wasting diseases such as tuberculosis, is any direct treatment required. One special condition, Addison's disease, is accompanied by a considerable lowering of the arterial pressure, presumably because of the absence of the internal secretion of the suprarenal glands, and considerable benefit has been stated to have followed in some cases the supply of suprarenal extract from without, but, beyond this, measures directed towards the raising of the blood pressure do not seem to have been advantageous.

Treatment of Diseased Arteries.—Arterial diseases may be divided into those that are inflammatory and those that are due to degeneration. The arteries may be involved in adjacent acute inflammatory processes, but here no special treatment of the vessels is required beyond the measures taken to combat the local inflammation. Inflammatory lesions of the arteries are also common in many acute infections, such as rheumatism, enteric fever and smallpox, but they are always undiagnosed and are not adapted for special treatment. They are important, as they are aften the starting-point of degenerative processes and may lead to local weakness of the vascular wall. Of all the inflammatory processes, those due to syphilis are the most important. These affect both

the inner and middle coats and lead to thickening of the vessels and obstruction to the flow of blood. They are also frequently followed by degeneration. An energetic treatment with iodides (5–20 gr. of potassium iodide three times a day), to which some mercury (½ dr. of Liq. Hydrarg. Perchlor.) may be added with advantage, will often result not only in an amelioration of the symptoms, but also in an actual lessening of the morbid changes in the arterial walls.

The degenerative processes in arteries are frequently in their origin inflammatory, and are generally accompanied by the development of a great deal of fibrous tissue, which is commonly regarded as a chronic inflammatory change. It is hopeless to expect any return to the normal in vessels in which there is excess of fibrous tissue or atheromatous changes, though fibrolysin, which has considerable influence on scar tissue, has been suggested as likely to reduce the fibrous element in arteriosclerosis. Any definite result from the employment of this drug yet remains to be proved, and it is a doubtful question whether any reduction of the fibrous tissue is to be desired, as it has usually arisen in replacement of degenerated muscle or elastic fibres, and so helps to strengthen a weakened wall. The main aim and object of the treatment of degenerated arteries must therefore be firstly, if possible, to prevent the spread of the morbid process, and secondly to relieve unpleasant symptoms. The degenerate changes are often, but by no means invariably, associated with increased arterial tension, and experimental and clinical experience seems to point to raised blood pressure as a potent factor in their production. Hence, to prevent further spread of this vascular degeneration, attempts should be made if the pressure is high to lower it, but unfortunately it is just in these cases where the arteries are already diseased that it is most difficult to produce any permanent alteration in the blood pressure. Still, considerable benefit may be derived from increased open-air exercise, a reduction in the time spent on business, and some release from its cares, and a careful regulation of diet, especially in the limitation of proteins. These patients are also usually decidedly the better for a course of iodides (Pot. Iod. 3 gr. three times a day), which may be continued over several months, and care should be taken that the bowels act regularly. The symptoms accompanying arterial disease are mainly caused by the resultant deficiency in the blood supply to certain organs of the body, which is accentuated by the liability of diseased arteries to spasm. For instance, there may be sleeplessness, mental impairment and temporary paresis from cerebral anæmia, dyspnœa from interference with the coronary circulation, coldness of the extremities, and sometimes gangrene when the arteries of the lower limbs are affected. Local treatment can do but little in these conditions, and the best results must be expected from efforts to fit the work to the capacity of the damaged machine. The mental work of a man with sclerosis of his cerebral arteries should be limited, and the physical exercise of one with coronary disease should be regulated by what can be done in comfort and without breathlessness. By such means a partly worn-out machine may deliver without discomfort a decreased output of work over a good many years, when an attempt to maintain the original level would have led to an early breakdown.

Aneurysm.—The proper treatment of an aneurysmal dilatation of an artery depends both on its nature and on its position. The general aim of treatment is to cause an obliteration of the sac by inducing the blood to coagulate in it, but while this principle is applicable to saccular expansions from the side of the vessel it is obviously unfitted for fusiform dilatations of any artery that cannot with safety be completely closed. Since aneurysms arise owing to some imperfection of the arterial wall which tends to act towards the blood as a foreign body, coagulation can generally be induced by causing the blood to stagnate for a sufficient time in the aneurysmal cavity. In the peripheral parts of the body this can be brought about by surgical means, *e. g.* the blood flow into the tumour may be prevented by compressing or tying the vessel between the sac and the heart, or where such operations are not suitable the supply of blood may be greatly decreased by ligature of the artery beyond the sac, which stops the through flow of blood. Such surgical measures are, however, impracticable for the great vessels of the trunk, the thoracic and abdominal aorta, where a sudden cessation of the blood flow is incompatible with the continuance of life. It is true that cases of complete obstruction of the descending thoracic aorta are known, but they are usually of congenital origin or, if they arise after birth, are of very slow development, so that ample opportunity is allowed for the establishment of a collateral circulation. The abdominal aorta may, it is true, be temporarily compressed by means of a suitable apparatus, but as a rule aneurysms of the great thoracic and abdominal arteries will require treatment fashioned on other lines to that suitable for the limbs. Still, surgical measures to promote coagulation have been devised and practised. For instance, foreign bodies (a considerable length of silver wire) have been introduced into the aneurysmal sac, and the inner surface of the sac has been scarified by the surgeon so as to cause it to act towards

the contained blood like a foreign body. Again, dilatations of such vessels as the innominate, left carotid or subclavian, may be treated by distal ligature, and aneurysms of the iliacs by temporary compression of the abdominal aorta. Then, again, coagulation in trunk aneurysms has been brought about by passing an electric current through the blood, two fine electrodes being introduced into the sac and a constant current passed through. Nevertheless, it is evident that the cases suitable for surgical interference are limited in number and that the treatment is fraught with special dangers.

Medical treatment may be divided into attempts to cure the aneurysm, to arrest its further growth or merely to relieve the unpleasant symptoms.

Treatment intended to cure the Aneurysm.—The fact that salts of calcium increase the coagulability of the blood has naturally led to their being recommended in the treatment of aneurysm; 10 gr. of the lactate may be given three or four times a day. Gelatine also increases the coagulability of the blood and was proposed by Lancereaux as a subcutaneous injection with the idea of assisting the coagulation in the aneurysmal sac. Lancereaux injected 3 oz. of a 2 per cent. solution of gelatine in 0·7 per cent. salt solution every third day into the flank or buttock for thirty or forty injections, and reported some very favourable results. Subsequent observers have failed to confirm this favourable opinion, perhaps because gelatine, as experiments have shown, quickens the blood flow. On the other hand, a decreased supply of blood to the sac might be supposed to favour the occurrence of coagulation there, applying the same principle as the surgical treatment of aneurysm in the limbs, and such a decreased supply would result from a general diminution in the blood flow. A decrease in the general blood flow would ensue in abstention from all bodily exertion, as in absolute rest in bed over several months, provided that active measures be taken to reduce the arterial blood pressure. This line of treatment was suggested long ago by Morgagni, who advocated in addition to absolute rest the abstraction of small quantities of blood, 6 to 10 oz., at intervals of a week. In more modern times it has been supported by Tufnell of Dublin, who in order to get sufficient reduction of the arterial pressure also advised that the intake of nutriment, both solid and liquid, should be reduced to the minimum necessary to support life. Tufnell's method has been widely practised, and it has been found possible to reduce the intake gradually to the following amounts and even to continue this very meagre diet for several months.

Breakfast.—2 oz. of bread and butter; 2 oz. of milk or tea.

Dinner.—3 oz. of mutton; 3 oz. of potatoes or bread; 4 oz. of claret.

Supper.—2 oz. of bread and butter; 2 oz. of tea.

That is to say, 10 oz. of solid food and 8 oz. of fluid in the twenty-four hours. Sometimes the absolute rest and restricted diet have been employed alone, sometimes conjoined with periodic blood-letting and, of course, the treatment may be combined with the administration of calcium lactate, potassium iodide or other drug. Good results have been recorded as the result of this régime apart from the mere amelioration of symptoms. Still, coagulation in the sac is by no means certain to follow; for instance, in a case seen by the writer as a student, which had been treated in this way for about eighteen months, the aneurysm, which from clinical evidence was supposed to be closed by laminated clot, ruptured about two years later, and at the post-mortem examination there was no evidence of any clot at all. There is naturally considerable difficulty in persuading patients to undergo such a very unpleasant régime, and the medical attendant has to consider whether he is justified in urging its adoption in the absence of any certainty as to a cure resulting.

Treatment designed to prevent further Extension of the Aneurysm.—Where the aim in treatment is not to bring about a cure, but merely to prevent the further growth in the size of the tumour and to guard against the giving way of its walls, the proceedings have to be somewhat similar to those that have been recommended with a cure as their object.

Aneurysm is caused by the giving way of a weakened spot in the arterial wall, or a general dilatation of the whole vessel, owing to the pressure transmitted by the blood. The weakening of the wall is due either to poisons or to degenerative processes following increased arterial tension; there may also be a sudden internal injury of the vessel wall from the strain of violent muscular effort. Naturally, the increase in size of an aneurysmal tumour depends directly on the pressure tending to expand it and inversely on the resistance to expansion offered by the wall of the sac and the surrounding structures. This resistance can be very little influenced by treatment, except by inducing coagulation to thicken the sac wall. Thus treatment has to be directed to diminishing the expanding force from within and to preventing, if possible, the extension of the morbid changes in arterial walls. Care has, therefore, to be taken to eliminate those conditions of diet and exertion which tend to raise arterial pressure and to cause vascular degeneration as well as to prevent toxæmia. As a very large proportion of cases of aneurysm arise from syphilitic disease of the vessels, the counteraction of any syphilitic taint is naturally

of the first importance. One can hardly expect treatment with antisyphilitic remedies to influence favourably a vessel wall that has already given way, yet there is a large amount of clinical evidence that the administration of iodide of potassium has a beneficial effect on the patient and his symptoms, especially when there is a past history of venereal disease. Thorough treatment may also be expected to prevent further vascular disease. It is, therefore, advisable to combine a course of iodides with measures calculated to reduce the blood tension. A course of treatment such as has been advocated for the cure of aneurysm of the thorax or abdomen frequently results in great relief of symptoms, and the disabilities do not return for a considerable time after the patient has returned to more or less ordinary life. One is justified in these circumstances in hoping that the vascular tumour, if no smaller, has at any rate not grown larger. To attain this end the régime does not require to be anything like so rigorous as has been proposed with the idea of producing a cure; for instance, the confinement in bed may be limited to six to twelve weeks, and the reduction of solid and liquid intake need not be such as to cause the patient discomfort. Coagulation may occur in the sac, though it is rather less probable than with the stricter régime. When the patient is again allowed to move about he must be warned of the danger of any sudden or violent exertion.

Symptomatic Treatment.—The symptoms of which the patient complains and for which he demands relief are mainly due either to stretching of the arterial walls or to pressure of the tumour on adjacent structures. They may be completely absent, but usually cause a good deal of discomfort. Pain may be caused by stretching of the walls of the aorta, and seems to be most severe and characteristic in disease of the ascending part of the arch, when it usually spreads over the right side of the chest and down the right arm to the fingers. But severe pain may also result from compression and erosion of bones, either vertebræ or ribs, and then is localised and aching in character. Pressure on nerves besides causing pain may lead to spasm, *e. g.* of the adductors of the larynx, or to paralysis. Pressure on the œsophagus causes dysphagia and on the trachea or bronchi brings on stridor or dyspnœa and later hæmoptysis owing to leaking of the aneurysm before rupture, while compression of the veins results in congestion and swelling behind the obstructed point. All these symptoms may be considerably relieved by rest in bed, and the relief seems to be materially increased by the administration of potassium iodide in doses of 3 gr. three times a day even where there is no syphilitic taint. Further measures are, however, usually required. For instance, pain has to be treated by local applications such as belladonna plasters, ice-bags or poultices, and in many cases these have to be supplemented by the hypodermic injection of morphia. Still, after a few weeks in bed and the above remedial measures many patients are able to get about again for a considerable period in fair comfort. Dyspnœa, which is often a troublesome symptom, whether it arises from pressure on the air tubes or from concurrent bronchitis, may also be usually much relieved by rest and the ingestion of potassium iodide. If the bronchitis is severe it may require treatment with expectorants such as ammonia, or, if there is much secretion, with belladonna. Sometimes the dyspnœa becomes urgent and is then best relieved by venesection. Hæmoptysis is often a sign of impending rupture into the trachea or a bronchus and necessitates absolute rest.

Spasm of the laryngeal adductors gives rise, of course, to urgent danger and may require tracheotomy to ward off death, but in less serious cases an attempt may be made to overcome the spasm by the inhalation of chloroform. Cough may be very distressing and is best treated by some form of linctus containing morphia. Nothing can be done directly for the relief of pressure on the œsophagus, with its attendant difficulty in swallowing, but this discomfort is often ameliorated with the other symptoms by rest in bed. The possibility of aneurysm as a cause of dysphagia must be remembered, as the passage of an œsophageal bougie may lead to fatal rupture. Now that the progress of food down the gullet can be seen by means of bismuth and the X-rays no bougie should be passed until the absence of a thoracic shadow with the X-rays has negatived the diagnosis of aneurysm of the descending aorta.

(See also article on *Thrombosis and Embolism.*)

A. M. G.

THROMBOSIS AND EMBOLISM

The Treatment of Thrombosis.—Thrombosis of any part of the vascular system is rarely, if ever, primary, so that it behoves the physician to bear in mind the possibility of its recurrence, and to take steps to prevent it whenever attending a patient suffering from any of the diseases with which it may be associated. There are many factors at work to produce thrombosis, and to treat the condition rationally it will not be out of place to mention them. They are—(*a*) Injury to the vessel wall, caused either by the local action of microbes or their toxins, or else by mechanical means. (*b*) Slowing of the blood stream, due either to some local obstruction or to general enfeeblement of the circulatory organs. (*c*) Altered composition of the blood.

The Prevention of Thrombosis.—The following general indications for the prevention of thrombosis arise from the consideration of the etiological factors.

(a) *To Eliminate and Neutralise Toxins.*—This is desirable from every point of view and especially to prevent thrombosis in infections in which it is likely to occur, such as puerperal sepsis and pyogenic infections generally. If of streptococcal origin, polyvalent antistreptococcal serum should be administered, and in the less acute cases an autogenous vaccine prepared. Whenever possible other infections should be treated on similar lines.

The patient should be encouraged to drink fluids freely, and in severe cases rectal salines, or better, continuous subcutaneous infusion of normal saline solution employed. Auto-intoxications such as gout should be treated in the appropriate way to eliminate the toxin.

(b) *To Maintain the Circulation at a Good Level.*—This is most likely to be required during the convalescence from a prolonged fever such as typhoid, and in cachectic conditions. General tonics should be prescribed—nux vomica or strychnine with a dilute mineral acid and bitter infusion—and as much nourishing food given as possible. Alcohol is indicated if there be much exhaustion, and a reliable preparation of digitalis if there be signs of marked cardiac failure.

Special care should be taken during the night when the circulation is at its lowest ebb. The patient should be kept warm, and encouraged not to lie with his legs crossed, as it is probable that the pressure exerted by the one knee on the superimposed femoral vein may be sufficient to obstruct the blood flow in it, and even to injure the endothelium, whereby thrombosis may be produced. It is a useful practice to have the legs of those who are confined to bed for any length of time gently rubbed three or four times a day. The venous circulation is considerably aided by this means.

(c) *To Maintain a Chemical Condition of the Blood Unfavourable to Thrombosis.*—The attempt may be made to diminish the amount of calcium salts in the blood. Sir A. E. Wright and Lieutenant Knapp have pointed out that a patient suffering from typhoid is kept almost entirely on a milk diet—milk containing a large amount of lime salts—and they advise the addition of sodium citrate to the milk (30 gr. to the pint) as soon as the danger of intestinal hæmorrhage has been surmounted. This alters the ionisation of the calcium, making it unavailable for blood coagulation, and at the same time the casein is made more easily digestible. All meat jellies contain a large amount of calcium salts, and are therefore better avoided. Citric acid (20 gr. every four hours for three or four days) or dilute phosphoric acid ($\frac{1}{2}$ dr. three times a day) may also be administered. The patient should drink plenty of natural lemonade or lime-juice. Addis questions the correctness of Wright's view; his experiments go to prove that the coagulation time of the blood is unaffected by citric acid given by the mouth.

Ammonia is believed to hinder blood clotting; Liq. Ammoniæ (20 min.) or Sp. Ammoniæ Aromat. (1 dr.) may be given frequently well diluted.

In conditions associated with cyanosis oxygen inhalations may be of service, for blood containing a large amount of CO_2 and deficient in oxygen clots readily. The application of six or seven leeches may be efficacious to prevent venous thrombosis; the beneficial effects of leeching may rather be due to the hirudin injected (which is a powerful anti-coagulant) than to the amount of blood abstracted.

The General Treatment of Thrombosis.—All that has been written under prophylactic treatment is equally applicable when thrombosis has occurred. The main indication in treatment now is to assist in the establishment of an adequate collateral circulation, so as to avoid the danger of gangrene from arterial thrombosis, and the effects of passive congestion from venous thrombosis. In cases of venous thrombosis it is of the utmost importance to guard against the danger of detachment of pieces of clot, which may give rise to fatal pulmonary embolism. This is best prevented by the maintenance of absolute rest, which is also an important factor in establishing the collateral circulation, so the necessity of it must be impressed on the patient.

Operative treatment is often necessary in cases of septic thrombosis, especially of the venous variety. In septic thrombo-phlebitis ligature of the vein is performed above and below the thrombosed area, and, if possible, the affected part excised. Gangrene, the result of arterial thrombosis, should be treated on ordinary surgical lines.

The Treatment of Special Forms of Thrombosis

Thrombosis of the Veins of the Lower Extremities.—This is the form of thrombosis most frequently met with. It occurs as a complication or sequel of infectious and general diseases, and also as the result of local causes such as an attack of pulebitis associated with varicose veins.

The patient must be sent to bed at once; he should lie on his back with the affected limb supported on a well-padded back-splint, the lower end of which should be raised about six inches. If the thrombus extend as high as the pelvic brim, the hip-joint should be fixed by putting the patient on a Thomas' hip-splint. A wire cage should be placed over the limb to remove the pressure of the bed-

clothes. The whole limb should be wrapped in cotton wadding or gamgee-tissue, and if there be much pain, a boracic fomentation, or hot lead and opium lotion (Liq. Plumbi Subacetat. 2 dr., Ext. Opii Liq. 4 dr., Aquam ad. 1 pint) applied on lint over the vein. In some cases more relief may be obtained by the application of dry heat, or of an ice-bag. The wadding and fomentations should be kept in position by a many-tailed flannel bandage.

If pain be not relieved by these local applications, aspirin (10 gr.) phenacetin (10 gr.), or in severe cases opium may be given internally. The patient should be cautioned against any sudden movement, and such acts as straining at stool and coughing prevented. The length of time the patient should stay in bed will depend largely on the severity of the attack. In a case of moderate severity, it is generally safe for him to get up at the end of six weeks, for by this time organisation of the thrombus will be well advanced. Active treatment should not be commenced until the temperature has been normal and all local tenderness has disappeared for three weeks. At first, slight, passive movements of the limb are executed; these are gradually increased, and after three or four days gentle massage is begun, avoiding the course of the vessel. After these manipulations have been performed for a week, the patient is permitted to move the limb himself, and a week before getting up the splint is removed. Before he gets out of bed, it is well to bandage the limb lightly from the foot upwards. He should be cautioned against standing for any length of time, and advised to rest with the leg raised; constipation must be avoided and no tight clothing allowed to constrict the limb. If, in spite of these precautions, œdema occur, it is best treated by careful massage, electricity and bandaging. A Crepon Velpeau bandage is much the best; it is elastic, soft, warm and porous. When a bandage of this material is used, it is rarely necessary to have resort to an elastic bandage or stocking.

Thrombosis of the Veins of the Upper Extremities.—This is treated in the same way as the similar condition of the lower limbs, except that the arm need not be put on a splint, but supported on a pillow at a slightly higher level than the body. Three weeks after all active manifestations have subsided the patient may be allowed up, the arm being kept in a sling for another two or three weeks.

Cerebral Sinus Thrombosis.—The non-suppurative form occurs occasionally in chlorosis and other states of exhaustion. The treatment is principally that of the anæmia together with the general measures mentioned earlier in this article. The patient should be kept in bed with the head almost flat, and not allowed to lie with the neck bent for fear of causing obstruction to the venous return which would favour an extension of the thrombosis. The suppurative form occurs most frequently in the transverse sinus as a complication of middle-ear disease. The treatment is largely surgical: the jugular vein is tied, the transverse sinus exposed, and the infected clot removed.

Portal Vein Thrombosis.—The non-suppurative form is usually associated with marked and rapidly recurring ascites, and with other signs of portal obstruction. Beyond paracentesis, the treatment is that of the causal condition (*e. g.* advanced hepatic cirrhosis); in some cases the Talma-Morrison operation may relieve the patient.

Suppurative pylephlebitis is generally fatal; the treatment is that of the primary disease. (See *Diseases of Liver.*)

The treatment of other forms of venous thrombosis is not given in detail, as it consists in carrying out the general principles described above.

Arterial Thrombosis

Thrombosis of the Cerebral Arteries. (See *Vascular Diseases of the Brain.*)

Thrombosis of the Arteries of the Extremities.—Arterio-sclerotic changes associated with old age and serious constitutional diseases may give rise to thrombosis of the arteries of the extremities. The arteries of the lower extremity are most frequently affected. A good deal can be done to prevent senile gangrene. The feet should be warmly clad in thick woollen socks, and old people should be careful to guard against any abrasion of the skin, which may allow the entrance of organisms. The same precautions ought to be taken by diabetics, as they, too, are specially liable to arterial thrombosis and gangrene. The treatment of the actual condition is the same as that of embolism of the corresponding arteries, to the description of which the reader is referred.

The Treatment of Embolism.—There are several varieties of embolism. In the ordinary use of the term, the embolus is understood to be a piece of detached thrombus, or vegetation from a cardiac valve. Fat embolism, air embolism, and embolism due to tumour cells, parenchyma cells, parasites, bacteria and foreign substances also occasionally occur.

Every precaution should be taken to prevent embolism. The general indications in treatment are the same as those already considered for thrombosis.

Pulmonary Embolism.—One of the branches of the pulmonary artery becomes blocked by a mass of clot dislodged from a vein. This is most frequently seen after operations (especially on the pelvic organs) and as a complication

of the puerperium. Everything possible should be done to prevent this disaster. After any major abdominal operation the patient should be kept quiet in bed for three weeks and cautioned against any severe effort or sudden movement. This is all the more important if the condition be an infective one. As much fluid should be introduced into the system as possible, and the other treatment described under the prevention of thrombosis carried out. In the cases in which pulmonary embolism has occurred, the patient usually appears to be making an uneventful recovery until one day—frequently about a week or ten days after the operation—extreme dyspnœa and cyanosis, suddenly appear, and death ensues in a few minutes.

The patient should be propped up in bed; oxygen should be inhaled, and also whiffs of ammonia vapour. Diffusible stimulants such as ether and brandy should be given subcutaneously, and atropine sulphate ($\frac{1}{100}$ gr.), strychnine sulphate ($\frac{1}{30}$ gr.), and adrenalin (10 min. of the 1 in 1000 solution) administered hypodermically. Hot fomentations should be applied over the heart. Trendelenburg and others have performed pulmonary arteriotomy, but so far the operation has not been successful. In slight cases, which are more frequently the result of cardiac thrombosis associated with heart disease, the above treatment should be carried out, the side may be strapped for the relief of pain, and the hæmoptysis which is often present treated on the ordinary lines.

Cerebral Embolism.—This is another serious form generally occurring as a complication of either acute or chronic endocarditis. The treatment is that of the primary disease and of the resulting paralysis.

Embolism of the Splenic Artery.—Strapping the lower ribs may relieve the pain. In infective cases an abscess may form which should be treated surgically.

Embolism of a Renal Artery.—The patient should be put on a milk diet. The pain and hæmaturia may be lessened by poulticing the loins or by dry cupping.

Embolism of the Mesenteric Arteries.—If the collateral circulation be not rapidly established, gangrene of the intestine occurs. The only treatment likely to save the patient is the resection of the affected loop of bowel.

Embolism of the Arteries of the Upper and Lower Extremities.—The popliteal artery is the most frequently affected. In embolism of an artery of the upper limb occurring in a young subject, an adequate collateral circulation may be established, but frequently gangrene results. As soon as possible the limb should be painted over with a solution of iodine (3 per cent.) in rectified spirit or acetone, and then enveloped in sterilised cotton wadding or gamgee-tissue, so that if gangrene occur, there may be no infection from the outside. The limb should be slightly elevated on an inclined plane and kept warm. Opium may be required for the relief of pain. If gangrene ensue, it is for the surgeon to decide the time and site of amputation. Arteriotomy with the removal of the embolus has been attempted in the more accessible arteries, and with the improved surgical technique introduced by Carrel may become the recognised method of treatment in the future.

Fat Embolism.—Fat embolism is sometimes seen as a complication of fractures and other injuries. It is less likely to occur, if the blood-vessels and fat in the affected area be injured as slightly as possible by the manipulations of the surgeon. The lungs being the principal organs affected, the treatment is that described under pulmonary embolism.

Air Embolism.—If a large vein be injured in the course of an operation, and air gain entrance into it, air embolism is produced. This most frequently occurs during operations on the neck. The surgeon should immediately apply digital pressure over the wound in the vein, and if urgent symptoms appear, an attempt may be made to force the air onwards by injecting normal saline solution into the vein, or it may be possible to force air out of the opening in the vessel by rhythmical compression of the thorax.

Air embolism produced as the result of the activity of such organisms as the B. ærogenes capsulatus, requires as such no special mention; the treatment is that of the primary infection.

P. H.

TREATMENT OF DISEASES OF THE BLOOD AND BLOOD-FORMING GLANDS

DISEASES OF THE BLOOD

Pernicious Anæmia

Pernicious anæmia is a well-defined clinical entity associated with a typical blood picture, but it has not been proved that the disease is essentially specific and dependent upon a constant cause. The fact that certain known poisons, such as that of the parasite bothriocephalus latus, can produce an anæmia almost exactly resembling pernicious anæmia, suggests that a variety of unidentified poisons may be

responsible for the disease, and hence the first step in treatment of any case must be an attempt to discover possible sources of poisoning.

The clinical course of pernicious anæmia strongly supports the view that it is a chronic infective condition and Hunter believes that it is due to a "specific hæmolytic infection" contracted from drains and favoured by the presence of long-standing oral and gastric sepsis which is usually of streptococcal origin. The common occurrence of alimentary disturbances together with the results in some cases of antiseptic treatment, certainly suggests that these have some intimate or even causal relationship to the disease. But whatever view be taken of the nature of pernicious anæmia, it must be recognised that acute, subacute and chronic cases occur and that all save the most acute show spontaneous remissions and relapses. Only careful observation and prolonged experience can justify pronouncement upon the value of remedies which may be employed, therefore, and improvement must not be allowed to arrest treatment.

1. *Investigation of the Case.*—Exclusion of the recognised parasitic causes of anæmias of pernicious type is necessary, and it is to be remembered that pregnancy and carcinoma of the stomach are sometimes associated with a similar condition. Careful investigation of possible infective foci must be made, particular attention being paid to the state of the teeth, gums and tongue, and an attempt should be made to isolate any predominant organism present. In cases with intestinal symptoms a bacteriological examination of the stools may reveal the presence of streptococci in unusual numbers, and whenever an organism which appears to be acting pathogenically can be isolated, whether it be from the fæces, the mouth or elsewhere, it should be used in preparation of a vaccine.

2. *General Hygiene.*—Rest in bed should be enjoined until recovery is evident, and fresh air is always important. The diet must be adapted to the gastro-intestinal condition, and in acute cases or during the acute stages of the more chronic types of disease solids are not usually tolerated. Gulland urges restriction to milk and farinaceous foods in such circumstances and prohibits all meal preparations until the patient is definitely recovering. Experience of each individual case will ultimately determine the diet which is most suitable, and dyspeptic symptoms are to be treated by the ordinary methods. When digestion is good and the patient is in a chronic stage as liberal a diet as possible may be allowed.

3. *Drugs.*—Administration of arsenic is certainly one of the most valuable methods of treatment in this disease. Liquor Arsenicalis is the preparation most commonly given, and commencing with 3 min. three times a day after food, the dose is generally increased by addition of 1 min. about every three days until 15–20 min. are being taken thrice daily if possible; but Hunter thinks that smaller doses up to 5 min. are equally effective. Some patients do not take arsenic well and in all cases symptoms of poisoning (nausea and vomiting, neuritis, pigmentation, etc.) must be watched for and use of the drug suspended if necessary. Even with the most tolerant it is advisable to allow occasional intermissions if large doses are being given, and during the periods of relative recovery the dose may be reduced to 2 or 3 min. The organic compounds of arsenic (atoxyl, orsudan, soamin, etc.) have not proved convincingly successful, and although recovery after intravenous injection of salvarsan is reported, most observers have found the result to be but transient benefit or even hastening of the end.

Iron is useless.

Glycerin by the mouth in doses of 2 dr. three times a day is said to have brought about recovery. Bone-marrow has been given in many different forms but is of doubtful value; certainly most of the commercial preparations are useless, and marrow should be obtained from fresh bones and given raw if the method is to have a fair trial.

Inhalation of oxygen has not been found useful by most observers.

4. *Disinfectant and Specific Treatment.*—Systematic attention to the infective foci already mentioned is of the first importance in the treatment of pernicious anæmia. The teeth must be scaled and the gums thoroughly disinfected, dead and carious teeth must be removed, and if there be definite pyorrhœa alveolaris it may be necessary to extract even apparently sound teeth. Hunter advises salicylic acid or salicylate of bismuth as a gastric disinfectant, and mercurials, such as the perchloride or grey powder, for the intestines. β-naphthol (10 gr. t.d.s. in cachets) or izal oil (2 min. in capsules before and after each meal) are excellent, especially in cases with diarrhœa. Gentle purgation is sometimes followed by improvement, but excessive looseness of the bowels is to be avoided.

In addition to the use of chemical disinfectants, vaccination may be employed to increase the resistance of the patient to specific infections associated with the disease. These, as has been said, are usually streptococcal, and the principles of vaccine therapy are discussed elsewhere.

Simultaneously with this, or even in absence of definite evidence of streptococcal infection, polyvalent antistreptococcic serum may be injected subcutaneously in doses of 10 c.c. on alternate days for two or three

weeks. Some observers maintain that normal horse serum is as useful as a specific immune serum, but it cannot be said at present that either is of proved value.

Gastro-intestinal disinfection, vaccine and serum therapy, and administration of arsenic may be employed simultaneously, but a second course of serum therapy must only be undertaken with due regard to the dangers of anaphylactic shock, since anaphylaxis, a condition of hypersensitiveness to the foreign serum, is developed about nine to thirteen days after an injection if no intervening injection has been given. The danger may be modified by subcutaneous injection of a small dose of serum (*e. g.* 1·0 c.c.) six to twelve hours before the remainder is injected, and all injections of the second series should be made very slowly.

Transfusion of blood from a healthy person has been tried with varying degrees of success. On the whole the results obtained are not encouraging, but the method has not yet been given a very thorough trial, for the technique is difficult and too advanced cases have usually been selected. Probably small and frequently repeated transfusions are to be preferred to a single large transference of blood, and this would practically prohibit the employment of vascular anastomosis. But ample experience in the treatment of other diseases by transfusion has shown that a syringe method (which cannot be described here) may be safely used by a skilled operator, and transfusion deserves to be tried early if at all. It should not be regarded as a last resource.

The improvement which has followed splenectomy in some cases of pernicious anæmia, does not appear to be either more marked or more constant than that which is frequently seen during spontaneous remissions of the disease.

5. *Special Symptoms,* other than those gastro-intestinal disorders which have already been mentioned and including such conditions as muscular cramps, hæmorrhages, cerebral disturbances and cardiac failure should be treated upon their own merits as they arise.

Secondary Anæmia

There is no specific treatment for the secondary anæmias. Recovery is dependent upon removal of the cause, and when this has been achieved, fresh air and good food are of greater importance than iron or arsenic. Both these drugs may help, but their effect on the secondary anæmias is in no way comparable to that of iron in chlorosis, nor even to that of arsenic in some cases of pernicious anæmia. And it is to be remembered that both exert a tonic action in cases quite devoid of anæmia. Complete investigation of every case must therefore precede treatment, and when the primary disease causing the anæmia has been discovered attention to this and to the general hygiene of the patient will do almost as much as can be done.

Hæmorrhage is responsible for some of the severest and most acute of secondary anæmias, and not only for those resulting from such conditions as trauma, hæmatemesis, and menorrhagia, in which the bleeding is sufficiently obvious to attract immediate attention, but for others in which its occurrence is apt to be overlooked. A large single hæmorrhage from an unsuspected lesion such as a duodenal ulcer may produce no more suggestive symptoms than an attack of faintness followed by melæna and an acute anæmia. The patient very likely fails to notice the altered blood in the stools, and if a correct diagnosis be not made repeated hæmorrhage or even perforation may occur. Smaller but recurrent hæmorrhages, as from hæmorrhoids, may be neglected as trivial and yet produce a profound anæmia, and the strain which such more or less continuous bleeding throws upon the bone-marrow may eventually exhaust its hæmatogenous function with a fatal result. Various measures for dealing with hæmorrhagic and posthæmorrhagic conditions are mentioned below under the headings *Purpura* and *Hæmophilia.*

Secondary anæmia is a usual accompaniment of *other diseases of the blood,* such as leukæmia and purpuras of unknown etiology, and the treatment is that of the primary disease.

The importance of *septic infection* as an essential or contributing factor in the production of anæmia is frequently overlooked but has been much emphasised by Hunter. He points out the very common occurrence and insidious nature of oral, gastric and intestinal sepsis, and any of these conditions may be responsible for aggravating an anæmia which is primarily due to some independent disease. On the other hand they or other infective conditions such as chronic suppurative lesions of the nasal sinuses may by themselves produce a secondary anæmia of any degree.

In each case appropriate and energetic treatment must be adopted. The perfunctory use of a mouth-wash is almost valueless in cases of pyorrhœa alveolaris; many will require complete removal of the teeth; in others extraction of stumps and scaling will be necessary and the sockets of such teeth as remain must be kept thoroughly clean by swabbing with hydrogen peroxide (20 vols.), and then applying a 2 per cent. solution of iodine in spirit each morning and evening. The gastro-intestinal condition usually improves as soon as the mouth is disinfected, but alkaline mixtures will aid in reducing gastric catarrh, and intestinal antiseptics such as salol and β-naphthol (10 gr. of

each t.d.s., the latter in cachets) should be given if intestinal symptoms are present. Wherever the infective focus may be, disinfection can only be properly completed by the establishment of free drainage, but when this has been effected the resistance of the patient to the particular organism concerned may generally be raised by use of the appropriate vaccine. Autogenous vaccines are desirable, and therefore cultures should be made from the lesion as soon as it is discovered and before active local measures have been adopted. (See *Vaccine Therapy*.)

Anæmia may also be produced by the *acute specific fevers*, particularly by diphtheria and acute rheumatism, and by *chronic septicæmic conditions* such as malignant endocarditis.

Tuberculosis is another common cause of anæmia and is apt to escape notice; it should always be borne in mind, and definite attempt must be made to detect or exclude it in obscure cases. There may be no localising symptoms in the early stages of the disease, but a characteristic constitutional disturbance with slight evening pyrexia may rouse suspicions which are justified by the discovery of physical signs or a positive reaction to one of the tuberculin tests. And it is clear that exact diagnosis is the first step towards adequate treatment. For the methods of treatment to be adopted in the case of particular lesions, the article dealing with each must be consulted.

Syphilis may be as potent a cause of anæmia and as difficult of recognition as tuberculosis. It is sometimes overlooked because no history is forthcoming or because there are no obvious local lesions. A relative or absolute lymphocytosis in the blood may excite suspicion and a positive Wassermann reaction is conclusive if the patient has not acquired some other tropical protozoal infection; but on the other hand syphilis may be present without being wholly responsible for the anæmia, and the possibility of complicating or coincident lesions emphasises the necessity for a very thorough investigation of each case.

Malaria and the *intestinal animal parasites* will seldom escape detection if the possibility of their presence is considered, and examination of the blood and fæces may exclude them or indicate appropriate treatment.

Anæmia of almost any grade may be produced by inorganic poisons, such as *lead* and *mercury*, or by the more obscure toxins of *nephritis* and *malignant disease*. Occasionally a diagnosis of carcinoma, latent as regards localising phenomena, may be arrived at by a process of exclusion in a patient at or past middle age with a progressive anæmia of secondary type and gradual loss of weight and strength. But *inanition* from any cause also tends to produce anæmia.

Chlorosis

Iron is a specific remedy for this disease and usually suffices to effect a cure in spite of unfavourable general conditions, but it is important to regulate the mode of life of the patient and to treat special symptoms which may occur. There are four chief considerations.

1. *General Hygiene.*—Exercise must be limited so as not to aggravate the symptoms, for while it is true that fresh air is essential to complete recovery it is equally true that lassitude and dyspnœa, faintness and palpitation, indicate the need of rest. The idea that chlorotics should take walking or other exercise in the open air is not infrequently responsible for delay in recovery in spite of the administration of iron. In severe cases with much cardiac dilatation it is well to keep the patient in bed for two or three weeks until definite improvement is apparent, and the inclinations of the patient will seldom mislead in the regulation of physical exertion. But fresh air and as much sunlight as possible are desirable throughout the *whole* course of treatment, and every use must be made of the increased opportunities afforded by improvement in the general condition.

Diet should be generous, including meat, but it must be modified if necessary in accordance with the gastric symptoms which are so frequently present. All dyspeptic conditions may be treated by the usual methods, but they seldom contra-indicate the immediate use of iron and this alone often suffices to remove them. The most common disorder is hyperchlorhydria, a condition of increased secretion of hydrochloric acid into the stomach, and hence most cases in which symptoms are present are benefited by administration of alkalies before meals. Fats in the diet tend to inhibit acid secretion and are therefore well borne, whereas proteins such as meat foods excite secretion and should be given in small quantities only until they are well tolerated. Oatmeal, apples, spinach and the leguminous vegetables are rich in iron, but as this element can always be added in medicinal form its presence in articles of diet is not of the first importance in immediate treatment of the disease.

The use of alcohol is both unnecessary and inadvisable.

2. *Iron.*—The best form is the Pil. Ferri (B.P.), and this should be given in gradually increasing doses—one pill (5 gr.) three times a day after food for the first week, two pills three times a day for the second week, and then three pills three times a day for at least two months. The number may then be gradually diminished in mild cases, but treatment should never extend over less than three months, and in most cases a course of six months is

advisable. Failure is sometimes due to defective absorption of iron owing to the form in which it is given (old, hard, insoluble pills), but much more commonly to administration of insufficient quantities of the metal, and chlorosis shows a great tendency to relapse. The patient frequently considers herself cured in a few weeks owing to the marked improvement which occurs as soon as treatment is commenced, but steady persistence is necessary, and even when health is completely restored it is well to keep the patient under observation and to re-administer iron at once if any symptoms reappear.

Some patients do not easily take iron. The physician should not be too readily discouraged, but if Pil. Ferri persisted with causes dyspepsia, Ferri Carbonas Saccharatus or Ferrum Redactum may be tried. Either may be spread as a powder upon bread and butter or made up in cachets or lozenges commencing with doses of 10 gr. and 2 gr. respectively three times a day and gradually increasing to three times these amounts. "Bipalatinoids" of iron (Oppenheimer), which contain ferrous sulphate and sodium bicarbonate in separate compartments of the same gelatin capsule, yield a freshly precipitated and readily soluble ferrous carbonate when acted upon by the gastric juice and may be tried in intractable cases. The per-salts of iron are more irritating than the ferrous salt in Pil. Ferri, and the scale preparations are weak but well taken by those whose digestion is easily disturbed. Organic preparations are more easily taken by many patients, but they are undoubtedly inferior in hæmatinic value to the inorganic salts. All forms of iron should be administered after food. Arsenic is said to be useful in some resistant cases, but only in combination with iron. It may be given in the form of Liquor Arsenicalis or as Arsenious Acid mixed with iron in a pill, *e. g.*—

℞ Liq. Arsen. ♏ iii
Sod. Bicarb. gr. x
Tinct. Calumb. ♏ xx
Aq. Chlorof. ad ℥ i.

To be taken three times a day after food in addition to Pil. Ferri.

or

℞ Liq. Arsen. Hydrochlor. ♏ iii
Liq. Ferri Perchlor. ♏ xv
Spt. Chlorof. ♏ v
Inf. Quass. ad ℥ i.

To be taken three times a day after food.

or

℞ Ac. Arseniosi gr. $\frac{1}{30}$
Pil. Ferri. gr. x
Ft. pil.

To be taken three times a day after food, the arsenic being omitted and the iron continued or increased as the patient recovers.

3. *Regulation of the Bowels.*—Constipation is a usual but not invariable symptom of chlorosis. Its correction is of essential importance and in obstinate cases it is well to start with a dose of calomel and then to give salines for a few days to a week. But the best regular purge for routine purposes is aloes, and this may be given as Pil. Aloes et Ferri (B.P.), or in a pill containing Aloes 2–4 gr., with Ext. Nuc. Vom. $\frac{1}{4}$ gr. It is well to modify the dose so that it may be taken regularly *every* night and serve to keep the bowels freely open each day. A pill containing Ext. Cascaræ Sagradæ 2 gr., and Ext. Nuc. Vom. $\frac{1}{4}$ gr., is sometimes sufficient and preferable, but each case must be treated according to its response.

It is said that intestinal antiseptics (*e. g.* β-Naphthol, 10 gr. t.d.s.) combined with the use of iron improve the results of treatment, but their administration is seldom necessary.

4. *Special Symptoms*, such as headache, palpitation, dyspnœa and œdema of the legs are often markedly relieved by administration of digitalis—small doses (3–5 min.) of the tincture three times a day. But any of these symptoms, if at all severe, indicates complete rest in bed.

The amenorrhœa of which so many patients complain is not an urgent symptom and menstruation will be re-established as the general condition improves. Menorrhagia need never cause alarm and always ceases when the patient is kept at rest in bed with other treatment appropriate to chlorosis. Probably the actual loss of blood is not a serious matter, for the total volume of the blood is greatly increased in this disease, and some observers have reported beneficial results from repeated small bleedings by venesection during the course of treatment by administration of iron.

Phlebitis, which most commonly affects the veins in the lower extremities, must be treated by absolute rest with elevation of the affected part and application of hot fomentations or belladonna liniment to relieve pain if necessary. Gentle massage may be commenced after two weeks, and the patient may be allowed to get up at the end of three to six weeks according to the size of the vein affected and the extent of spread of thrombosis. Continued massage and firm bandaging will assist the establishment of an adequate collateral circulation if any œdema of the leg remains.

Neuralgias may be treated by the usual methods and generally clear up spontaneously as the anæmia disappears.

Leukæmia

The treatment of a disease which has, according to our experience, an inevitably fatal issue is apt to prove disappointing unless we recognise

those variations in its type which influence the immediate prognosis. In considering the treatment of leukæmia it is necessary to remember, therefore, that different cases of the disease vary greatly in acuteness or chronicity as well as in the nature of the tissues chiefly affected. As regards the latter, intermediate types appear to exist, but the two main groups—myelogenous and lymphatic—are fairly distinct, and as a rule the lymphatic cases run the more rapid course and are less amenable to treatment. Roughly it may be said that a case is unfavourable in proportion to the acuteness of its onset and course, the degree of anæmia and the preponderance, both relative and absolute, of lymphoid over myelocytic elements in the blood. Acute lymphatic leukæmia is seldom even checked, but chronic myelogenous leukæmia may present such remissions under treatment as to simulate complete recovery. In the former group of cases treatment is chiefly directed against symptoms, particularly hæmorrhage; in the latter a more definite attack can be made upon the pathological condition of the tissues which appear to be primarily affected.

1. *General Hygiene* should be regulated according to the suggestions made for cases of pernicious anæmia.

2. *Drugs.*—Arsenic often proves very valuable, producing marked though temporary improvement. The Liquor Arsenicalis is a convenient preparation and should be pushed to the limits of tolerance as in the treatment of pernicious anæmia (*q. v.*). In some cases the organic compounds such as atoxyl, soamin and orsudan, do good, and any of these preparations, preferably soamin, may be administered subcutaneously, 10 gr. doses dissolved in sterile distilled water being injected on alternate days until ten doses have been given. Owing to the tendency of this treatment to produce optic atrophy smaller doses (1–3 gr.) are now usually recommended, but hope and fear go hand in hand and some risk may be considered justifiable in treating so fatal a disease. Salvarsan and neosalvarsan have not hitherto proved of definite value.

Quinine in large doses has been advocated, and in a case under care of Dr. Drysdale, an acute myelogenous leukæmia with intestinal symptoms, naphthalene tetrachloride in doses of 7 gr. at first every three hours and later every two hours, produced such marked benefit as to constitute an apparent cure. But the patient relapsed and died from cerebral hæmorrhage a few months after leaving hospital.

The use of benzol, recently introduced by von Kiránye, has produced some brilliant results in cases both of myelogenous and lymphatic leukæmia. It would be premature at the present time to make a final pronouncement upon its value, especially as regards the permanence or duration of improvement, but benzol promises better results than have been obtained with any other drug. It is best administered in gelatin or keratin capsules each containing 0·5 gm. of chemically pure benzol and 0·5 gm. of olive oil. At first two capsules are given twice a day after the principal meals, and the dosage is then gradually increased until 3–5 gm. are being given daily. The larger doses may cause albuminuria or hæmaturia, and watch should be kept for other symptoms of benzol-poisoning such as giddiness, headache, abdominal pain, vomiting, purpura and anæmia. When the stomach is intolerant to benzol, smaller doses, up to 2 gm. in twenty-four hours, may be given subcutaneously mixed with an equal amount of olive oil, but this method is painful and has not been much used. The optimum dose must be determined by the tolerance and progress of each individual case and very frequent examinations of the blood are advisable. No patient should be treated with benzol unless close and continuous observation is possible. There is a tendency to some increase in the number of leucocytes in the blood at first, but after a little time (usually about two weeks) a fall begins and is accompanied by improvement in the general condition of the patient, diminution in the size of the spleen or glands, and increase in the number of red cells and amount of hæmoglobin in the blood. It is advisable to cease administration of the drug as soon as the leucocyte count falls to about 12000 cells per c.mm., as the diminution will tend to continue and might be pressed too far. One of the signs of benzol-poisoning is leucopænia. In cases of myelogenous leukæmia the differential leucocyte count gradually tends towards the normal, and in the most favourable cases myelocytes may disappear from the blood altogether, but in lymphatic leukæmia the proportion of mononuclear cells remains high, even when the total leucocyte count has reached normal limits.

Administration of benzol does not contra-indicate the simultaneous or successive employment of other methods of treatment, and these, particularly the use of X-rays, are always to be kept in mind.

3. *X-rays.*—Hitherto this has undoubtedly been the most generally effective method of treatment. It is suitable for all cases of myelogenous leukæmia, whether early or late, and for chronic cases of the lymphatic type. The rays are applied to the ends of the long bones, the sternum, spleen, liver and to any enlarged glands that may be present. One part may be exposed at each sitting and various methods are advocated, some workers advising short exposures (ten to fifteen minutes) every two or three days, others preferring

longer exposures at weekly intervals. The exact details of the technique employed should be determined by an experienced operator. But whatever practice be adopted it is important to avoid excessive applications, for after preliminary improvement this leads to progressive deterioration of the red blood cells, and ultimately, the leucocytes also being greatly diminished in number, the blood picture of pernicious anæmia may be reproduced. To guard against this it is therefore necessary to control the use of the rays by frequent hæmatological observations, attention being paid not only to disappearance of the excess of white cells, but also to the number and hæmoglobin-content of the red cells. Deterioration of the latter is an indication for immediate cessation of X-ray treatment.

The improvement in clinical condition, however marked, is probably only temporary, and after subsequent relapse X-ray treatment is usually less successful or even without effect. Occasionally X-rays appear to aggravate the symptoms and induce headache, lassitude and pyrexia; in such cases the use of the rays must be diminished or discontinued.

4. *Other Methods of Treatment*, mainly directed to the spleen, have so far proved to be useless, as might be expected when it is remembered that all the clinical and pathological evidence points to the involvement of the spleen as being a secondary phenomenon in the disease. Splenectomy is an unjustifiable and fatal operation in leukæmia.

Transfusion of blood from a healthy person has been tried by Crile and he cannot recommend it.

5. *Special Symptoms*, such as hæmorrhage, gastro-intestinal disturbances and cardiac failure should be treated by the usual methods.

Leukanæmia

This term has been applied to a group of cases in which the blood picture presents some of the features of leukæmia combined with others characteristic of pernicious anæmia. Most of such cases are probably examples of acute myelogenous leukæmia or of the last stages of the chronic form, and treatment should be carried out along the lines indicated above, although it is usually of little avail. Attention has already been drawn to the fact that excessive use of X-rays in cases of leukæmia may lead to a leukanæmic condition of the blood and benzol is likewise contra-indicated.

Chloroma

Practically no treatment is known for this condition, which is characterised by the presence of greenish, subperiosteal, lymphoid masses and the blood picture of lymphatic leukæmia. In the present state of our ignorance those methods which have been advocated for leukæmia should be applied and special attention should be directed to the more urgent symptoms such as hæmorrhage and pain. But the disease is invariably and usually rapidly fatal.

Purpura

Purpura is merely a symptom and rational treatment can only follow an accurate diagnosis of the condition to which it is due or with which it is essentially connected. Nevertheless, in a comparatively large number of cases purpura is the principal or even the only symptom, and no definite conclusion as to the etiology of these has yet been reached. There should be no satisfaction in labelling such cases "idiopathic" or "simplex," or in saying that they are manifestations of a latent rheumatism, for treatment remains purely empirical. But when some graver lesion underlying the purpura is discoverable this will be the first consideration in treatment, and no special therapeutic attention need be paid to the purpura itself except in so far as it may indicate a general hæmorrhagic tendency. The treatment here suggested, therefore, is not directed against subcutaneous hæmorrhage alone, but against spontaneous bleeding from any part of the body.

1. *General Hygiene.*—Complete rest in bed is advisable, at least until the purpura is definitely fading. The diet should be adapted to the general condition and the bowels should be kept freely open.

2. *Drugs.*—Arsenic is sometimes remarkably effective in cases of "purpura simplex," and small doses usually suffice, although it may be necessary to push the drug. Oil of turpentine also appears to have some value as a hæmostatic. It is usually given thrice daily in doses of 5–15 min. emulsified in mucilage of acacia (1 dr.). But Eustace Smith recommends that in the case of fairly robust individuals doses of 2–4 dr. may be given, mixed with an equal quantity of castor oil, one hour after food each morning. It is the non-purgative doses of intermediate size which are apt to cause nephritis. Calcium lactate 15 gr. three times a day for three days, sulphuric or aromatic sulphuric acid 15–20 min. three times a day, liq. adrenalin. hydrochlor. 5–30 min. every three or four hours, and liquid extract of ergot $\frac{1}{2}-1$ dr. three times a day, are all used, but without constantly convincing results. If there be good grounds for supposing the purpura to be a rheumatic manifestation it is rational to administer salicylates, but it is to be remembered that purpura is sometimes an indication of intolerance of this drug.

3. *Blood and Serum Therapy.*—Administration of human or animal serum by oral, subcutaneous or intravenous routes has proved effective in many cases of purpura and other spontaneous

hæmorrhages. Fresh human serum is preferable, but if this cannot be obtained animal serum, fresh drawn or already stocked, may be used. Normal horse serum, anti-diphtheritic serum and anti-streptococcic serum appear to be equally valuable, and doubtless owe their virtue to the same common constituent. Subcutaneous and intravenous injections are to be preferred to administration by the mouth or per rectum, but the danger of inducing anaphylactic symptoms by the use of animal sera must be remembered. The patient is immune to such phenomena if successive doses of serum are separated by intervals of not more than a week. If longer than this has elapsed, the intravenous method must not be employed and a small dose (*e.g.* 1·0 c.c.) should be given subcutaneously six to twelve hours before the remainder, the subsequent injection being made very slowly.

Within recent years improvements in technique have rendered practicable the direct transfusion of blood from a healthy individual into the circulation of a patient. Transfusion is to be preferred to serum therapy for several reasons. It is more effective in arresting hæmorrhage which is not under surgical control, and by replacing all the lost elements of the blood, it tends to relieve the hæmopoietic tissues when they are temporarily exhausted. Further, transfusion involves no wastage of the blood taken from the donor, and the risk of bacterial contamination during the process of transference is reduced to a minimum. In cases of extreme urgency the time which would be occupied in separating the serum is saved by the use of whole blood, but unless the loss of a few hours is likely of itself to prove fatal, the natural compatibility of the blood of the two persons concerned—patient and donor—should be determined by examination for isoagglutinins and isohæmolysins. These bodies are present in a small percentage of persons, and are probably a source of real danger in transfusion. Small amounts (10–20 c.c.) of blood or serum may be effective for hæmostatic purposes, but if the patient has bled freely, ½–1½ pints may be transfused from a healthy donor and the bulk of circulating fluid may be further increased, if necessary, by infusions of normal saline solution, or better, of Ringer's fluid.

When the patient is evidently suffering from loss of fluid, and so long as the source of the bleeding can be controlled, rectal, subcutaneous or intravenous injections of normal saline solution may be resorted to immediately and stimulants may be given freely. If, further, the tissues of the patient may be expected to make good the loss of specific elements of the blood, transfusion of large amounts will not be necessary, but where hæmorrhage may recur owing to imperfect control of the local lesion, the volume of the blood and the strength of the heart-beat are only to be increased by other means than transfusion of human blood when their diminution threatens to lead to a fatal termination.

4. *Local Treatment.*—In addition to the general treatment recommended above certain local measures for the control of hæmorrhage may be adopted. Direct pressure is one of the best, but it is not always applicable, either because the bleeding point is out of reach or because the blood oozes from a wide surface which presents no obvious lesion. Adrenalin (1 in 1000) is a useful local application, particularly to the mouth, gums or nose. In cases of hæmatemesis adrenalin may be given in 1 dr. doses by the mouth every hour for several hours. For hæmorrhage from the bowels Pil. Plumbi c̄ Opio is honoured by time, but the important constituent is probably the opium, and in any severe case of hæmorrhage, provided there be no acute cardiac failure, a hypodermic injection of morphine is valuable for stilling the patient.

5. *Joint Pains* are a frequent accompaniment of the idiopathic purpuras, and whether or not they be regarded as evidence of acute rheumatism, salicylates, particularly aspirin, may be employed in their treatment.

6. *Henoch's Purpura* is a sufficiently well-defined condition to deserve special mention, although its etiology is still obscure. The patient, usually a child, should be kept in bed, and nothing but iced milk should be given by the mouth. If the pain is very severe a hypodermic injection of morphine should be given, and small doses of opium (*e.g.* Tinct. Opii 3 min., or Pulv. Ipecac. Co. 2 gr., or Pulv. Cret. Arom. c̄ Opio 8 gr., for a child of twelve years) may be given regularly afterwards if necessary. Potassium iodide has been recommended, and a case is recorded in which adrenalin (1 in 1000) 2 min., and Liquor Arsenicalis 3 min., given every four hours, apparently dispelled the symptoms with remarkable rapidity.

In some cases at least there is evidence to suggest that a streptococcal infection may play a part in the disease, and a careful search should be made for infective foci, particularly in the tonsils. If such be found—and an attack of tonsillitis may have heralded the approach of characteristic symptoms—active disinfectant measures should be employed against it, and a vaccine prepared from the predominant organism may be administered as a prophylactic against further attacks. Tonsils which show signs of inflammation should be removed during a quiescent period.

Antistreptococcal serum has been advocated by some writers, but probably its value is not

dependent upon its specific nature and serum therapy may be employed on the lines laid down above.

The symptoms of Henoch's purpura frequently resemble those of intussusception very closely, and subcutaneous hæmorrhages may escape notice or only appear several days after the onset of pain. It may therefore be very difficult to distinguish between these conditions, and a further difficulty arises in that the two are sometimes associated, intussusception apparently being excited by the presence of submucous hæmorrhages in the intestine or by violent peristaltic movements. Rectal examination and palpation of the abdomen with the patient under a general anæsthetic may reveal the presence of an intussusception, but in the absence of definite physical signs in a doubtful case it is advisable to keep the patient under observation without immediately opening the abdomen.

Hæmophilia

1. *General Precautions.*—All persons known to be, or suspected of being, subjects of this disease should be most carefully protected from injury from their infancy onwards. The indirect violence of exertion may induce hæmorrhages into the joints and subcutaneous tissues and is therefore as much to be avoided as direct wounding of the skin. Extraction of teeth and other operative procedures are attended with grave risks and should only be undertaken in urgent circumstances and after due consideration. The fact that a boy of hæmophilic stock has never suffered from immoderate bleeding affords no guarantee of safety, for the hæmorrhagic tendency does not always manifest itself in the first few years of life.

Residence in a warm climate is advisable, especially during the winter, and hydrotherapy, particularly sea-bathing, seems to be useful as a prophylactic against spontaneous hæmorrhages. If sea-bathing is impracticable regular cold douches and cautious massage may be substituted. An ordinary diet may be taken and a liberal supply of milk should be included.

In regard to the question of marriage the law of transmission of hæmophilia must be remembered. The rule is that females of hæmophilic stock, while not themselves "bleeders," transmit the disease to the majority of their male descendants. A careful study by Bulloch and Fildes of all the reported cases shows that there is no sufficient evidence for the belief that females may occasionally be true bleeders, or that males, whether themselves affected or not, may transmit the disease; and so far as the consideration of marriage is concerned such doubtful possibilities may be neglected. Few hæmophilic males ever marry, however, and it is inadvisable that any should do so, but the risk which they incur is confined to the direct and indirect results of their personal injury. It is otherwise with the females of affected families, for they tend to be exceptionally fertile and may perpetuate the disease indefinitely through the female line to the males of any subsequent generations. It matters not that their brothers may be free from the taint, so long as their mother's brothers, or maternal grandmother's brothers, exhibited it. Marriage of all such women must be strongly condemned.

2. *Drugs.*—Calcium is the most vaunted drug for hæmophilia, and appears to be valuable in some cases, although much difference of opinion still exists with regard to the theory of its action. Doses of 15 gr. of the lactate should be given three times a day for not more than three days. Continued administration is said to diminish the coagulability of the blood, and hence treatment may be ordered for a day or two each week during the intervals of hæmorrhage. In the case of a patient who is actually bleeding a large initial dose (1 dr.) may be given immediately. But calcium is not readily absorbed, particularly, it appears, in some cases, and for these Wright commends a mixture of calcium lactate and magnesium carbonate in equal parts. Subcutaneous injections of calcium have been tried without special success, and the chloride causes local sloughing, while the lactate causes pain.

Wright recommends internal administration of extract of thymus, up to twenty 5 gr. tablets being given daily. Ovarian extract, thyreoid extract, adrenalin, turpentine, gelatin and perchloride of iron have all been given internally without definite benefit.

Inhalation of carbon dioxide (which may be generated in an ordinary Kipp's apparatus or supplied in cylinders) is said to check hæmorrhage and may be repeated as often as necessary. (Wright.)

3. *Serum Therapy* is the most valuable form of treatment at our disposal at present. Fresh serum, either human or animal, is the best, but if this cannot be obtained, the normal horse-serum now stocked, or even antidiphtheritic or antistreptococcic serum, when no other is at hand, may be used. Intravenous administration (10–20 c.c.) is the most effective method and the minute puncture necessary may be made where it can be easily controlled subsequently. Subcutaneous injection (20–30 c.c.) entails risk of hæmorrhage into the tissues, and ingestion by the mouth cannot be relied upon. It is stated that intravenous injection once per month suffices to prevent spontaneous hæmorrhages and even to render operative procedures safe, but the development of ana-

phylaxis must be borne in mind if animal sera are used, and injections at so long intervals are only safe when immunity to the particular serum employed has been maintained by repeated small injections at short intervals (less than a week).

Crile has found that direct transfusion from a healthy person gives good results, but the difficulties of the operation must be greatly increased when it is performed on a hæmophilic, and the syringe method should be employed in preference to a vascular anastomosis.

4. *Local Treatment.*—A large variety of local applications have been tried without constant success, *e. g.* 1 to 2 per cent. solution of calcium chloride, adrenalin (1 in 1000), 1 to 2 per cent. cocaine, gauze compresses soaked in 5 per cent. sterile gelatin and the actual cautery. Whenever possible local pressure should be employed, but the most efficient method of dealing with hæmorrhages from the skin or mucous membranes is the application of fresh blood (human or animal) or of extract of some highly cellular organ such as the thymus or testis, after removal of all blood-clot lying superficial to the bleeding point. Wright recommends the following method of preparation of this "physiological stryptic": Extract chopped thymus or testis (from calf or lamb) with ten parts of normal saline solution containing a trace of sodium bicarbonate. Add 1 per cent. carbolic acid and allow to stand for twelve to twenty-four hours if possible, but strain at once if necessary. To the strained fluid add 0·25 to 0·5 per cent. calcium chloride (weighed as crystals) and then apply directly to the bleeding surface on a plug of wool or lint with as much pressure as possible.

5. *Joint Affections* are treated by complete rest. Puncture of the joint is only indicated if the pressure of the effused blood becomes unbearable. After a few days, gentle massage should be applied to the proximal part of the limb, the joint being untouched and unmoved. Some degree of permanent deformity is practically unavoidable. A. E. S.

DISEASES OF THE SPLEEN

Splenic Anæmia

Although it is by no means proved that all the cases described under the title splenic anæmia are examples of one and the same disease, yet they form a fairly well-defined clinical group, and for purposes of treatment they may be considered together so far as our present knowledge goes. It need hardly be insisted that differential diagnosis from other diseases in which enlargement of the spleen, anæmia, hæmatemesis, etc., occur, must precede any rational therapeutic measures.

1. *General Hygiene.*—Fresh air is no less essential than in the treatment of other blood diseases, and rest and diet must be adapted to the symptoms of each case; there are no special indications. If the enlarged spleen causes much discomfort a belt may be used to support it.

2. *Drugs* do not appear to be of much value, but arsenic is generally used and is probably the best; it should be given in gradually increasing doses as in pernicious anæmia. Iron is useless and quinine and boracic acid have been advocated without much success.

3. *X-rays* applied to the spleen are certainly useful in some cases, causing a diminution in size of the organ with coincident improvement in the blood picture and clinical condition. But the results are palliative rather than curative, and excessive exposure to the rays may do more harm than good. It is therefore important to examine the blood at frequent intervals during this treatment and to regulate the applications accordingly.

4. *Splenectomy* has been followed by some remarkable successes and should be considered in every undoubted case of the disease. Whether recovery is really permanent remains to be seen, but it has been reported even in advanced cases with cirrhosis of the liver and ascites (Banti's disease). It must be remembered, however, that the operation is often attended with great difficulty and has an immediate mortality of about 12 per cent. in the best hands, the chief risk being due to hæmorrhage after separation of adhesions between the enlarged spleen and adjacent parts. The general condition of the patient must largely influence the result of surgical interference, and therefore the operation should be performed as early as is consistent with careful diagnosis. If the spleen is already much enlarged and fixed, a preliminary course of X-ray treatment may render its removal less difficult.

5. *Special Symptoms* must be treated as they arise. The most troublesome are hæmorrhages, particularly from the stomach, and here the blood comes from minute erosions of the veins without any ulceration recognisable by the naked eye. The usual principles governing treatment of hæmatemesis must be followed, but in view of the fact that there is no macroscopic ulceration, diet may be augmented more rapidly than usual and the Lenhartz method should always be adopted.

Acholuric Jaundice.—There are two types of this condition, congenital and acquired; and both present as their chief features splenomegaly, jaundice (which may be intermittent), anæmia and debility, while the red blood corpuscles show a pathognomonic increase of fragility. Splenectomy has produced uniformly good results in both types of case, and the absence of adhesions renders the operation relatively simple. It is not yet

possible to say whether the relief afforded by splenectomy constitutes a complete cure, but there is ground for hoping that it may do so; no other methods of treatment are of any value.

Von Jaksch's Anæmia

This condition, sometimes known as *Pseudoleukæmia Infantum* or *the Splenic Anæmia of Infancy,* is certainly quite distinct from the splenic anæmia of adults, although, like that disease, it is probably not to be regarded as a definite pathological entity. Attention must be paid to the general hygiene and the diet should be such as is indicated in rickets, including eggs, raw meat-juice and a liberal supply of milk. Iron and cod-liver oil should be given. Syrup. Ferri. Phosph. Co. is very palatable and efficient, and cod-liver oil is well taken when mixed with extract of malt in the proportion of one to four. Application of X-rays to the spleen has been advocated, but this is purely empirical and of doubtful value. Splenectomy should never be performed.

Erythræmia (*Splenomegalic Polycythæmia*)

Nothing is known concerning the etiology of this disease and at present treatment is very unsatisfactory. Bleeding gives marked but very temporary relief, and application of X-rays to the spleen, though usually of more permanent value, is not successful in all cases. In view of the suggestion that erythræmia is due to a hyperactivity of the erythroblastic elements of the bone-marrow analogous to the excessive leucoblastic activity in leukæmia, the effect of X-rays applied to the long bones is worth trying. A case has been reported in which treatment with benzol produced temporary benefit, the red blood cells falling from 9,000,000 to 6,700,000 per c.mm. This drug certainly deserves a trial, and should be employed according to the suggestions made for leukæmia. Splenectomy is never justified.

Other Diseases of the Spleen

The functions of the spleen are such that its removal from an otherwise healthy individual causes little or no disturbance of health. It is not surprising, therefore, that disease of the organ is usually manifested only by enlargement, and as primary splenic diseases are rare, attention is more often directed to the spleen for purposes of diagnosis than for treatment.

But while the primary condition is being treated, splenic symptoms may call for immediate relief. Acute stretching of the capsule may be diminished by free purgation, and pain due to perisplenitis by local application of hot poultices or of antiphlogistine. A chronically enlarged spleen may be supported by means of a suitable belt and pad; sometimes its size may be reduced by application of X-rays, and in some cases, even when the spleen is only secondarily involved, as in syphilis and malaria, improvement follows its removal.

The conditions dealt with below are those in which the spleen is wholly or mainly responsible for the symptoms of the patient.

Movable Spleen.—This is seldom found without some other morbid condition and is most commonly a part of a general visceroptosis. For purposes of treatment both the condition of the spleen itself and the symptoms which it is causing must be considered. If the organ be healthy save for its abnormal mobility it may generally be disregarded. It is doubtful whether belts applied to the abdomen will keep a spleen of normal size in its proper place. If the pedicle of the spleen becomes strangulated, immediate operation is indicated and the organ should be removed, but apart from this emergency surgical intervention may be justified by continuous pain, discomfort and anxiety, splenopexy or splenectomy being performed.

Rupture of the Spleen is a dangerous and not uncommon accident. Surgical treatment is always indicated and removal of the spleen is advisable if it is not obviously diseased. But if it be enlarged by long-standing disease suture or plugging of the rupture is to be recommended.

Thrombosis of the Splenic Vein sometimes occurs as a result of local pressure or sepsis and gives rise to enlargement of the organ and recurrent hæmatemesis—a condition suggesting and sometimes practically indistinguishable from splenic anæmia. Splenectomy is the proper treatment if the patient can stand the operation.

Abscess of the Spleen demands appropriate surgical treatment unless it occurs as a part of a general pyæmia, in which case local interference will not be adopted unless the general condition of the patient permits operation and encourages hope of recovery.

Primary Tuberculosis of the Spleen occasionally occurs and may cause massive enlargement. Good results following splenectomy have been recorded, but in all cases, whether operation is justifiable or not, general treatment should be carried out along the lines appropriate for other cases of tuberculosis.

New Growths and Cysts (simple, dermoid or parasitic).—When a diagnosis of primary splenic tumour can be made splenectomy is indicated. The event is a rare one and the exact nature of the lesion cannot always be determined before operation.

A. E. S.

DISEASES OF THE LYMPH GLANDS AND THYMUS

Acute Lymphadenitis.—Since this condition is the result of the transmission of organisms by lymph coming from an infected wound, the

primary focus of infection must be carefully looked for and when found appropriately treated. It sometimes happens that the glandular enlargement only appears after the primary infected wound has completely healed, but in these cases a scar is frequently to be found somewhere within the lymph area drained by the gland. Where the primary wound can be found it should be carefully cleansed, opened if pus be present, and dressed antiseptically. If on the fingers it is wise to avoid carbolic dressings, since if these be kept continually applied there is considerable risk of gangrene supervening. Most of the cases of gangrene following the use of carbolic acid dressings have occurred where weak solutions of 1 in 50 or 1 in 100 have been kept in contact with wounds overnight, the anæsthetic properties of the carbolic acid giving the patient no warning of the serious change that is occurring.

Glycerine of belladonna should be painted over the inflamed glands and hot fomentations applied, in this way not only will pain be relieved, but the resulting hyperæmia will lead to flooding of the tissues with opsonins and leucocytes. Where necessary a splint may be applied if rest cannot otherwise be ensured. As an alternative treatment passive hyperæmia may be induced by the application of a Bier's bandage—in those cases where the anatomical position of the inflamed gland allows of such a procedure—or Klapp's suction bell may be employed.

The exhibition of a saline purge and a tonic mixture will constitute all that is usually required in the way of general treatment.

If *suppuration* has occurred an incision should be made in the line of cleavage of the skin overlying the gland and the abscess opened. Hilton's method (*i. e.* the insertion of a pair of dressing forceps and opening the blades to secure free evacuation without the danger of wounding large vessels) may be of use where the glands are situated deeply in regions such as the neck or axilla; but if any of the gland remain it is wise to remove this entirely, since multiple foci of suppuration are frequently present in such residual portions of gland and considerable delay in healing will otherwise occur. For this purpose a finger or sharp spoon is all that is necessary, and a drainage tube should be inserted for a day or two.

The treatment of bubo is considered under the heading of *Venereal Lymphadenitis* (*vide infra*).

Venereal Lymphadenitis.—1. Glandular enlargement may be regarded as an almost constant phenomenon in primary and secondary syphilis; it is rarely met with in the tertiary stage of the disease. Suppuration does not occur unless in the primary stage some pyogenic organism in addition to the spirochæte gains access to the part. General anti-syphilitic treatment must be instituted, but no local treatment is called for.

2. A bubo, secondary to a soft sore, usually shows itself about fourteen days after the appearance of the sore, and unless treatment on definite lines is instituted *suppuration* is not likely to be long delayed.

(*a*) Where in the *early stages* inflammation is not acute, rest, with the application of a pad and firm Spica bandage is all that is requisite.

(*b*) Where *softening* of the glandular swelling threatens excision of the affected group of glands is better treatment than incision. Care must be taken to remove sufficient of the surrounding subcutaneous tissue to ensure against injury to the gland, otherwise healing by first intention is not likely to occur.

(*c*) Where an *abscess* is already present the best results follow the use of a flushing curette introduced through a small incision. Thorough flushing with a 1 in 4000 corrosive sublimate solution must be followed by scraping away the remains of the gland and the introduction of iodoform emulsion into the abscess cavity. Free incision is to be avoided as it is likely to be followed by the formation of an indolent ulcer.

3. A bubo occasionally occurs in the course of gonorrhœa, the local treatment differs in no way from that of acute adenitis ending in suppuration (*q. v.*).

Chronic Lymphadenitis results where long-continued toxic absorption or microbic infection is taking place. Here also a careful search must be instituted for the primary focus. In hospital practice the presence of pediculi in the head is one of the most frequent causes of cervical adenitis. Examination of the throat for tonsillar enlargement and adenoids, and of the mouth for the presence of carious teeth, must never be omitted in cervical cases. Mr. Warwick James, from an extended experience in the dental department at Gt. Ormond Street, finds that cervical glands are palpable in all children, but when healthy they can only just be felt and are freely movable. When irritated by *toxic* products they become enlarged and soft, but usually remain movable, and are only slightly, if at all tender. If definitely infected by *organisms*, they are tender, more or less fixed (periadenitis), and perhaps show softening at one point. After removal of the teeth in these cases and cleansing of the mouth the glands undergo contraction and remain as small firm nodules. Tubercle bacilli appear to be able to flourish in glands whose resistance has thus been lowered by chronic infection. Should enlargement of glands persist after removal of the primary focus of infection the possibility of tuberculosis must not be lost sight of.

Where the primary source of infection can be found, its removal is usually attended by more

or less gradual subsidence of the glandular enlargement and no local treatment directed to the glands is necessary. If an ulcer of the skin or dermatitis is found it must receive appropriate treatment.

Since secondary tuberculous infection is likely to occur in chronic cases of inflammatory enlargement, should the glands show no tendency to subside, or worse still, go on increasing in size, the more serious condition must be suspected, and suitable measures carried out for its treatment (*vide infra*).

It is not always easy to detect suppuration where glands are deeply placed, such as when lying beneath the sternomastoid, but if the patient be kept under close observation room for doubt cannot long exist.

Tuberculous Lymphadenitis is one of the most common of the chronic affections of childhood. The disease may affect any group of glands, but most commonly involves the bronchial and mesenteric groups among the more deeply seated glands, the cervical among the more superficial ones. Seeing that the organism obtained from affected glands is almost always of the bovine variety, infected *milk* must be regarded as the chief source of the disease. For this reason milk from tuberculin-tested cows, where such is available, should alone be used. When this cannot be obtained, all milk should be pasteurised or boiled, but the decrease in nutritive value which these methods entail renders such milk a less efficient substitute.

There is little doubt that in cases of tuberculosis of the cervical glands infection occurs through the tonsils and nasal part of the pharynx. Mr. Sampson Handley has suggested that much might be done to diminish the likelihood of infection if a practice were made, in the case of all town-bred children, of washing out the nasal part of the pharynx daily with a weak antiseptic. A fountain-pen filler forms an admirable means of introducing half a dozen drops or so of a weak solution of glycothymoline into each nostril night and morning. If the tonsils are enlarged they should be painted with a weak solution of iodine (0·5 per cent. solution).

While tuberculous cervical glands remain small, isolated and mobile no surgical interference is essential. But where signs of matting of the glands (periadenitis) or any tendency to softening is present, or where the overlying skin is becoming inflamed, surgical intervention can rarely be safely delayed.

In the earlier stages medical treatment will consist in placing the child in the best hygienic surroundings and, as regards locality, Margate and Ramsgate have a well-earned reputation. Sea air is not, however, essential, and children do very well in elevated open country. Internally the pharmacopœial Syrupus Ferri Iodidi is often of the greatest value, and doses of 20–30 min. may be given in a little water three times a day to a child of five. If the iron produce constipation, or the child is poorly nourished, one or two tablespoonfuls of cod-liver oil should be given morning and night in addition. There can now be obtained a crystalline preparation of malt extract and iodide of iron which is especially useful in cases of this kind. Arsenic in small doses (Liq. Arsenicalis 1–3 min.) either given alone or in conjunction with the iodide or phosphate of iron is often of the greatest value. Local applications such as iodine or hot fomentations to the affected glands are on the whole best avoided; they frequently appear to hasten softening. It is well to inform ignorant mothers and nurses not to handle or rub the swellings. If the enlarged glands are situated in a part like the groin, where they are exposed to considerable movement, rest must be enjoined, or secured where necessary by means of a splint and bandage.

In the early stages tuberculin has been largely employed apparently with a certain measure of success. In the later stages of the disease, where the glands lying in condensed fibrous tissue may be undergoing central caseation, the use of tuberculin cannot be defended. In these cases it is impossible for the protective substances formed in the body to reach the bacilli within the diseased gland.

Koch's New Tuberculin is the form usually employed. Either the human (T. R.) or the bovine (P. T. R.) variety may be used. The initial dose should be about $\frac{1}{100,000}$ c.c. T. R. ($\frac{1}{50,000}$ mg. solid substance), which is given hypodermically in isotonic solution. If the opsonic index is not determined it is usual to repeat the dose after eight days, and if after three injections no improvement results, the bovine tuberculin, P. T. R., may be substituted. The dose is gradually increased (controlled by temperature, pulse-rate and a consideration of constitutional symptoms) till something like $\frac{1}{1000}$ c.c. ($\frac{1}{500}$ mg. solid substance) is reached. By some vaccinists the dose is increased till in the case of an adult as much as 20 mg. is given.

Operation will be indicated in cases where matting of the glands has occurred and where suppuration threatens or is already present. Not only should all the enlarged glands be removed, but the whole layer of fat and fascia in which they are lying should be resected, as in this way alone can the surgeon ensure complete removal of infected, though not visibly tuberculous, glands. The operation is often one of some difficulty; it always involves opening the carotid sheath if carried out on the lines indicated, while any but a practised surgeon runs considerable risk of injuring the accessory nerve, which may escape recognition

lying embedded, as is so frequent in these cases, in a dense mass of fibrous tissue or of glands.

Hodgkin's Disease.—The exact nature of this disease still remains undetermined. Evidence is not wanting to show that it may follow repeated or chronic infection. It is, therefore, the duty of the medical attendant to seek diligently for any local source of infection. As the glandular enlargement usually first shows itself in the neck, a most careful examination of the mouth, nose and pharynx should never be omitted, and any infective focus must receive immediate attention. Should the disease when the patient is first seen be limited to one group of glands surgical removal of the glands in question should in addition be advocated. In some of the cases thus treated the disease appears to have undergone partial arrest, in others there has been no recurrence for several years. Surgical interference cannot be recommended where there is definite evidence of constitutional disturbance; hence operation is negatived—save for the relief of pressure—where there exist multiple glandular tumours, splenic enlargement, fever or severe anæmia. Of the remedial agents available in the treatment of this disease arsenic is probably the only one worthy of serious consideration. Whether it acts by attacking the infecting organism (if such exist) or by increasing the nutrition, and hence the resistance, of the tissues can only be conjectured. Fowler's solution is the form in which the drug is usually administered. Beginning with 3 min. three times a day after meals, the drug may be gradually increased till toxic effects as evidenced by itching of the eyes, silver furring of the tongue, garlic odour of the breath, or epigastric discomfort be noticed. Great diminution in the size of the glandular swellings sometimes occurs after the use of even such small doses of atoxyl as $\frac{1}{2}$ gr. twice weekly. Care must be taken not to " push " the dose of the organic arsenical compounds, since, unless due caution and discrimination be employed, optic atrophy may result. Should disturbance of vision be complained of, or any diminution of the visual field be recognised, the drug should be discontinued. Sodium cacodylate forms another useful vehicle for the exhibition of arsenic : it may be given once daily in $\frac{1}{2}$ gr. doses hypodermically. A remedy of which the writer has had no personal experience is phosphide of zinc which has been used with benefit in this disease; it is usually prescribed in pill form, the dose being $\frac{1}{20}$ gr. three times a day.

Remarkable results follow the application of X-ray treatment. Where the applications are persisted in the glandular swellings can often be kept under control, though it is doubtful if cases are actually permanently relieved.

It is too early yet to speak with any certainty of the effect of radium or salvarsan.

Lymphosarcoma. — Lymphosarcoma, when arising in lymph glands, usually affects the cervical or axillary group. So soon does the growth burst through the capsule and infiltrate surrounding structures that excision is rarely possible. Even where excision can be performed the outlook is very grave, as other glands soon show evidence of rapid enlargement. Little can be expected from the use of Coley's fluid in this dread disease. If it be decided to inject Coley's fluid (the Lister Institute supplies new Coley's fluid in 2 c.c. phials) it is usual to start with doses of $\frac{1}{4}$ or $\frac{1}{2}$ min. diluted with sterile distilled water. Slight malaise may follow the injection, but in susceptible patients a rigor and a rapid rise of temperature to 104° may occur. If there is no definite reaction the dose is repeated the following day, and the dose is increased by $\frac{1}{2}$ min. a day till a reaction occurs. From this point onwards the dose must be governed by the temperature, the object being to get a definite rise of temperature without serious constitutional disturbance. The maximum dose is rarely carried beyond 10 or 15 min. and treatment is usually continued until it is clear that no improvement is taking place or till the swelling disappears. The best results obtained with Coley's fluid have been in cases of spindle-celled sarcomas.

Several cases have been reported in which beneficial results have followed the use of radium. The best results are obtained where radium is buried within the growth for twenty-four hours.

In the late stages of the disease anodynes such as aspirin (15 gr.), phenacetin (5–10 gr.), or morphia ($\frac{1}{4}-\frac{1}{2}$ gr.) are necessary for the alleviation of pain.

Diseases of the Thymus Gland.—Almost the only disease of the thymus gland (if indeed the expression may be allowed) which is likely to benefit from medical treatment is the so-called status lymphaticus or lymphatism. The disease is more correctly regarded as one in which there is an overgrowth of lymph tissue throughout the body and in this overgrowth the thymus participates. The disease derives its chief interest from the startlingly sudden death to which its victims are liable if subjected to the most trifling operation or accident. Hence the recognition of such cases becomes of paramount importance.

Children suffering from lymphatism are usually pale and flabby. The tonsils are frequently enlarged and adenoids are likely to be present. A mild degree of rickets is not infrequently to be detected. The lymph tissue throughout the body is increased, but since the superficial lymph glands rarely show

any noticeable enlargement the disease is rarely diagnosed with certainty during life. In some cases the thyreoid gland is increased in size and in others a definite swelling in the suprasternal fossa, due to excessive enlargement of the thymus, has been noticed during expiration. X-ray examination may be of assistance in recognising this condition. An extensive area of dullness may be discovered over the upper part of the sternum and neighbouring portions of the chest wall, but it is almost impossible to distinguish such an area of dullness from that caused by tuberculous mediastinal glands. A somewhat more definite indication of the existence of an enlarged thymus is provided by the occurrence in such children of definite attacks of dyspnœa—the so-called thymic asthma.

If the condition is diagnosed, or strongly suspected, small doses of arsenic and iron should be given and any errors of diet corrected. If the child be rickety or syphilitic the underlying disease must be treated. Children tend to outgrow lymphatism, but as they appear to be unduly susceptible to infective diseases they should be kept as far as possible from the risk of infection. All operations save those of necessity must be avoided, and many deaths under anæsthesia, in the case of children, are assigned to this condition. Cold baths should not be allowed and excitement of all kinds is bad for the subjects of this malady. The use of fresh raw thymus gland obtained from sheep has been advocated, and as much as half an ounce of the extract of the gland in the form of tablets may be given to a child daily. Those who advocate this line of treatment argue that the thymus in undergoing hypertrophy is responding to some abnormal stimulus, and that if thymus extract be given in sufficient quantity the gland will gradually subside.

During an attack of thymic asthma, oxygen may be inspired and cardiac stimulants exhibited. In some cases intubation performed with a tube sufficiently long to reach the bifurcation of the trachea has been successfully performed, in others the thymus has been partly resected, or drawn forwards, and fixed to the fascia over the sternum.

Laxatives may be freely used. Some cases appear to have benefited by X-ray treatment.

It has been advised in the case of children subject to this distressing condition that the nurse should be warned not to allow the child to throw his head back and to do all in her power to prevent crying or screaming—truly a difficult task!—as anything which tends to increase the pressure which the gland exerts on surrounding structures, or which leads to congestion of the gland, may precipitate an attack. C. E. L.

TREATMENT OF DISEASES OF THE ALIMENTARY SYSTEM

DISEASES OF THE TEETH AND GUMS AS A FACTOR IN GASTRO-INTESTINAL DISEASES

Diseases of the gastro-intestinal canal which are secondary to diseases of the teeth and gums are, in most instances, due to infection caused by the continual swallowing of micro-organisms from septic conditions of the latter.

These conditions are—

1. *Pyorrhœa Alveolaris*, which is by far the most common.
2. *Advanced Caries*, especially when septic roots are present.
3. *Alveolar Abscesses*, in which the pus is draining into the mouth.
4. *Stomatitis*, due to general lack of oral cleanliness, especially with regard to dentures, etc.
5. *Certain irregularities of the teeth* such as overcrowding, which allow the lodgment and consequent decomposition of food.

1. **Pyorrhœa Alveolaris.**—The first thing to be done here is carefully to scale the teeth and then remove all the septic stumps and "dead" teeth. The "dead," or pulpless teeth, always remain a likely source of fresh infection. They have lost the blood supply to the pulp and can only receive a limited supply of nourishment from the partially destroyed periodontal membrane, consequently in the present state of our knowledge it is impossible to render them perfectly healthy. All gold crowns and bridges must be removed, as they almost invariably cause damage to the periodontal membrane. In considering the further treatment it is advisable to divide the cases into two classes—

(*a*) Those patients who are not as yet showing general symptoms.

(*b*) Those patients who, in a greater or less degree, are showing signs of toxæmia.

(1) In the first class a radiograph should be taken to ascertain the amount of rarefying osteitis present in the alveolar process, and the depth of the pockets round the teeth should be ascertained by a fine probe. The amount of pus that can be squeezed out of each pocket and the amount of gingivitis present should be noted.

By these means we can further subdivide this class into—

(i) Slight cases in which the amount of osteitis is small and the pockets shallow.

(ii) Advanced cases in which there is a con-

siderable amount of rarefying osteitis present and the pockets are deep.

In the slight cases conservative measures can be tried. It may be admitted at once that there is no known method of bringing about the reformation of the absorbed bone and so effecting a cure. All we can hope to do is to *arrest* the disease and prevent recurrence by getting rid of the pockets. Now considering that the disease is probably predisposed to by a loss of resisting power of the alveolar process due to our modern cooking and consequent lack of proper mastication, as pointed out by Mr. J. F. Colyer, the patient must be instructed to correct this as far as possible by living on fibrous foodstuffs requiring a certain amount of mastication, and this must be carefully and conscientiously performed. By this means an increased blood supply is brought to the alveolar process and its "tone," or resisting power, is increased. Further the patient should be instructed to carry out at least three times a day, and if possible before and after each meal, the following treatment: First to squeeze out the pus and debris from the pockets round each tooth by pressure between finger and thumb; then to wash his mouth out for two or three minutes with the following mouth-wash—

℞ Liquor Potassæ ʒ vi
Acidi Carbolici ʒ iv
Liquor Cocci ʒ ii
Aquam ad. ℥ viii

One teaspoonful to half a tumblerful of warm water. The object of the Liquor Potassæ is to dissolve the mucus and so allow the carbolic acid to act as an antiseptic. This having been done, the patient should carefully brush all surfaces of the teeth and gums, especially the latter, with a hard tooth-brush and soap, in order to scarify them, using an up and down, as well as a to and fro, movement. A powder should not be used, as it is liable to "cake" in the pockets and act as an irritant. Lastly, the mouth should be washed out with a hydrogen peroxide mouth-wash, using the 10 per cent. solution, for two or three minutes. The whole process should occupy about fifteen minutes.

The dental surgeon must assist the patient by keeping all the teeth very carefully scaled and polished, taking great care to injure the gingival margin as little as possible during the operation. All areas of stagnation, viz. places where, owing to the destruction of the interdental papillæ, food is very liable to lodge and decompose, must be carefully attended to. If the gum papillæ are soft and spongy they should be cut away with a pair of sharp curved scissors, and in the same way all "pockets" round the teeth must be removed. The importance of this cannot be too strongly insisted upon because if they are left they speedily become reinfected. Equally important is it to insist upon the patient breathing through the nose, experience having shown the impossibility of ever arresting the disease in mouth-breathers.

At the end of six months another radiograph should be taken to ascertain whether the disease has been arrested by these means. If it has the patient may retain his teeth; but only then under careful supervision, as there is always a strong tendency to recurrence. If the disease is still spreading, as shown by the extent of the rarefying osteitis, it must be treated as a severe case. In discussing the treatment of severe cases, in which there is no evidence of a general toxæmia, the question arises—is there any justification for condemning the remaining teeth? I agree with Mr. J. F. Colyer in thinking that there is, because, in the first place, the patient's resisting power may at any time become broken down by some other intercurrent disease, and that disease, plus the oral sepsis, may not improbably lead to serious, or even fatal, results; and in the second place, if the bony absorption is allowed to progress until the teeth drop out, there is practically no alveolar ridge left for the retention of dentures, whereas if they are extracted early a good ridge results to which dentures can be comfortably fitted. Granting the disease to be incurable, it is not wise to put off the wearing of dentures to the last possible moment and then find them always inefficient and uncomfortable because of the absence of a proper ridge. It is far wiser to anticipate their adoption by a few years, and by so doing make for efficiency.

(2) *Cases Showing General Toxæmia.* In these cases all the affected teeth should be removed as a general rule. Extensive extraction having been decided upon, the question arises—should all the teeth be removed at a single operation? When a large number of teeth are removed at one time there remains after the operation a large raw surface, through which septic absorption may take place. Cases have been reported in which death has followed from this cause a few days after the operation. When, however, one considers the large number of these operations which have been done, and the very few cases in which anything untoward has happened, it is clear that the risk is very small. Unfortunately very few dental surgeons at the present time make any attempt to cleanse the area of operation before operating. If all the tartar is removed carefully a few days before, and the gums, especially the spaces between the teeth, carefully painted with a 2 per cent. solution of iodine in rectified spirit immediately before the operation, the risk is reduced to a minimum. It would seem to be the best plan to remove all the teeth at one time

in those cases where the patient is dangerously ill from septic absorption. In such cases vaccines may be used to advantage for tiding the patient over the danger period—the ten days following the operation.

In cases where there is no such urgency, it is better to remove all the molars at the first operation and then a week later to insert dentures. When the first wounds have healed the incisors can be removed and replaced on the dentures, leaving the bicuspids to aid in their support until the patient is thoroughly accustomed to retaining them in position. The great advantage of this method is that the teeth standing when the dentures are first inserted give the correct bite.

The generally accepted view of the vaccine treatment of pyorrhœa alveolaris is that it merely deals with the symptoms due to the toxæmia; it does nothing to assist the cure of the disease itself; the pockets round the teeth and the areas of stagnation remain and quickly become reinfected. The rarefying osteitis is possibly checked during the period in which injections are being made, although there is as yet no direct evidence even of this. When the vaccine treatment is stopped, the rarefying osteitis certainly progresses with a return of the toxæmic symptoms.

The electrical, or ionic, treatment is also of little permanent use because though it may sterilise the pockets it does not get rid of them, and they invariably become reinfected.

2. **Advanced Caries.**—Here the unsaveable teeth must be removed and the saveable ones filled. "Collar" crowns should be avoided, as they almost invariably lead, sooner or later, to damage of the gingival margin and periodontal membrane. In adults all functionless (*i. e.* unopposed) teeth must be made functional by suitable dentures. In children, not only must all unsaveable teeth be removed, but their antagonists also. In a case, for instance, where the four lower molars are unsaveable, it is useless to leave the four upper. The loss of their antagonists has rendered them useless for masticating purposes. They consequently are no longer self-cleansed by the mastication of the fibrous foodstuffs and quickly become carious and gingivitis is set up around them.

3. **Alveolar Abscesses.**—If the tooth is unsaveable, it should be removed; if saveable, the abscess must be thoroughly opened up and drained.

4. **Stomatitis.**—The cause should be removed; a suitable mouth-wash prescribed, and the patient instructed in oral hygiene. (See *Stomatitis.*)

5. **Irregularities of the Teeth. Overcrowding.**—Here the alveolar process is not large enough to accommodate all the teeth properly in a regular arch. This is due very frequently to lack of development of the jaws owing to nasal obstruction, whereby one or more teeth are crowded out of the proper alignment, and form stagnation areas where food must lodge and decompose.

Treatment consists of either—

(*a*) Expansion of the arch.

(*b*) Extraction of the instanding teeth.

With regard to expansion, it must be remembered that the appliances used for this are liable merely to swing the teeth out on a point at their apices, so that if the arch is much expanded the articulation of the teeth is ruined. However, in suitable cases, expansion is the best method. When nasal obstruction is the cause, expansion of the jaws can be brought about by simply removing the obstruction and rendering the nasal cavities again functional. In severe cases, extraction is the only satisfactory method.

Finally dyspepsia may arise in patients with healthy mouths due to inefficient mastication, owing to the loss of several teeth. These teeth can be replaced by—

(*a*) Dentures.

(*b*) Bridges.

In favour of the first is the fact that they can be easily removed and cleaned.

In favour of the second is the fact that they are fixed and consequently preferred by many patients. They are, however, very difficult, if not impossible, to construct in such a way that they can be kept clean. Their use almost invariably leads, sooner or later, to chronic suppurative periodontitis (pyorrhœa alveolaris).

F. St. J. S.

STOMATITIS

The term stomatitis is very wide and indefinite. It includes an inflammation which may spread over the whole surface of the mucous membrane covering the gums and cheeks, or which may be more or less limited to the gingiva. In the former case it is generally acute, and is very much commoner in children than in adults. In the latter case it is generally chronic, is most common in adults, and is almost invariably associated with periodontal disease (see *Pyorrhœa Alveolaris*).

Stomatitis in children very commonly follows measles; in a large number of children examined by the writer, the great majority of those suffering from stomatitis had had measles.

Children with nasal obstruction, and who are consequently mouth-breathers, almost invariably suffer from stomatitis in a greater or less degree. It is also frequently associated with gastrointestinal trouble, or with dentition, when it is usually localised around the erupting tooth.

Stomatitis in very young children can often be traced to dirty feeding-bottles, or faulty

oral hygiene. In adults, a chronic form of stomatitis is often seen under artificial dentures, especially those made of red vulcanite. This is frequently due to lack of cleanliness, and quickly disappears when this is remedied and the plates left out a few days. In some cases, however, the writer has only been able to cure this condition by inserting a new denture made of black instead of red vulcanite.

Several forms of stomatitis have been described, but before considering the treatment of these in detail a few general remarks should be made.

In treating stomatitis it is of the utmost importance that proper nasal breathing should be established. Any nasal obstruction, if present, must be removed. If this is not done an acute case may not only become chronic and very resistent to treatment, but the inflammation may spread to the periodontal membrane setting up chronic suppurative periodontitis (pyorrhœa alveolaris) with all its attendant evils both local and general.

All septic teeth which cannot be made healthy must be removed. Gastro-intestinal trouble must be treated.

1. **Catarrhal Stomatitis.**
2. **Aphthous Stomatitis.**
3. **Ulcerative Stomatitis.**

The treatment of these three forms may be taken together. In young children the mouth should be carefully wiped round with glycerin of borax, applied on a piece of soft linen or lint which should afterwards be destroyed. In older children, and in adults, the mouth-wash recommended by Dr. Still is one of the most suitable—

℞ Pot. Chlorat. gr. vii ss
Boracis gr. x
Glycerin ʒ ss
Aq. Rosæ ad. ℥ i
As a mouth-wash.

Aphthæ or ulcers which persist may be swabbed over with a solution of silver nitrate 5 gr. to the 1 oz., or pure silver nitrate may be applied. This is best done by heating the end of a blunt probe to redness, rubbing it over a stick of silver nitrate, and touching the ulcer with this after it has been allowed to cool.

Chlorate of potash internally is very beneficial. Children may be given 4–8 grs. according to age. Adults 10–15 grs.

A tonic may be advantageously prescribed with this, such as—

℞ Tinct. Ferri Perchloridi ʒ ii
Pot. Chlorat. gr. lxxx
Spiritus Chloroformi ♏ lxxx
Glycerin ʒ iii
Aquam ad. ℥ viii.

Two tablespoonfuls to be taken every four hours.

A purge should be given.

4. **Gangrenous Stomatitis or Cancrum Oris.**—The treatment here must be prompt and energetic if the child's life is to be saved. The whole of the affected area must be thoroughly and completely removed until healthy bleeding tissue is reached. The raw surface must then be thoroughly cauterised, either by strong nitric acid, pure carbolic or the actual cautery.

5. **Parasitic Stomatitis (Thrush).**—The mouth should be carefully wiped round with a piece of lint dipped in glycerin of borax after each meal. An alkaline mouth-wash should be prescribed—

℞ Acidi Carbolici ʒ iv
Liquor Potassii ʒ vi
Aquam ad. ℥ viii.

One teaspoonful to half a tumblerful of warm water as a mouth-wash frequently. In the case of a young child the mouth can be swabbed with a piece of cotton-wool dipped in this.

Chlorate of potash should be given internally.

It must be remembered that the disease is infectious, and all feeding-bottles must be carefully sterilised. The mother's nipples should be treated after each suckling with a mild antiseptic.

6. **Mercurial Stomatitis.**—An antiseptic mouth-wash should be prescribed. The drug should be discontinued until the local condition shows marked improvement. If the pain is severe Pulv. Opii Co. should be given at night.

F. St. J. S.

DISEASES OF THE SALIVARY GLANDS

Increase of Secretion.—This is due to a variety of causes, thus it may be (1) apparent in paralysis of the muscles of swallowing in septic tonsillitis and pharyngitis, with septic teeth and their results, and in the various forms of stomatitis—here the cause must be dealt with by appropriate means; (2) *Toxic* due to pilocarpine, mercurial poisoning and uræmia; (3) *reflex* in pregnancy and hysteria; it may even be a normal condition in children. Atropin is of real benefit in reflex salivation, a single hypodermic injection of $\frac{1}{100}$ gr. should be given rather than the continued administration of tincture of belladonna.

Decrease of Secretion may be (1) toxic in fevers, particularly typhoid—here mouth-washes containing lemon juice are indicated; (2) due to atropin poisoning. Here a dose of pilocarpine hypodermically acts well once the poison is discontinued, decreased secretion is frequently noticed in arterio-sclerosis, occurring in comparatively early life—its occurrence materially increases the gravity of the prognosis. In this connection the condition described by the

late Sir Jonathan Hutchinson as "xerostomia" may be noticed; it is very common in women, and as resistant to treatment. Little is known of its causes. Pilocarpine or the galvanic current would appear to be the only lines of treatment.

Inflammation. Acute Primary Epidemic-parotitis.—The general treatment of this condition will be found under infective fevers. Attention may be here directed to the very remarkable results of the inunction of iodex (Pigm. Iodi M. and J.) on the affected glands. All swelling and signs of inflammation are removed in about forty-eight hours by gentle inunction every two hours. Nothing definite is known as to any alteration in the period of infectivity by this treatment. A modified Trendelenburg position has been suggested with a view to avoiding "sympathetic" inflammation of the reproductive glands.

Secondary Acute Parotitis.—This is known to be associated with septic infections below the diaphragm. With more active surgical intervention its frequency is diminishing, the early occurrence of suppuration as well as the frequency of a burrowing outside the "parotid fossa" should be remembered. A very early incision will not usually be regretted. On the other hand, many hold that it is always secondary to a dry infected mouth whether the primary cause of infection is above or below the diaphragm, also that many resolve without incision.

Chronic Parotitis is usually caused by stones in the ducts, which should be surgically dealt with. In addition to stones, a chronic fibrinous inflammation of the ducts has been described. It is worthy of note that tuberculosis of the salivary glands is of extreme rarity (this must not be confounded with tuberculosis of lymph glands in their neighbourhood).

Symmetrical Enlargement of Lacrimal and Salivary Glands.—This has been described as "Mikulicx's disease." It would appear to be of very complex nature, and due to increase of lymph tissue, possibly a lymphoid hyperplasia. X-rays together with arsenic and iodides in full doses at the same time have given good results.

Occasional Enlargement of Salivary Glands.—This is of quite frequent occurrence, especially in the submaxillary gland; it is usually observed in a single gland. It is said to be usually caused by calculus in the duct, but the author has seen no less than nine cases in children under twelve, where no calculus or other cause of obstruction could be found. In all these cases the intermittent swelling disappeared ultimately.

Salivary Calculi.—Symptoms of their presence closely resemble the above. Swelling of the gland (usually the submaxillary) occurs immediately after a meal; it is usually painful (salivary colic), and the swelling slowly disappears, returning after the next meal taken. The calculus is usually single, and can be felt 10–20 mm. from the submaxillary caruncle. They are usually single and are probably due to bacterial infection as in the case of gall stones. They can be readily cut down on and removed.

Ranula.—This cystic swelling in the floor of the mouth is usually due to cystic degeneration of one of the glands in the floor of the mouth. When congenital it is usually due to imperfect development of the duct of the submaxillary or sublingual gland. Treatment is by cutting down on the cyst, and removing as much of the cyst wall as possible, the rest being left to granulate.

Growths.—So-called "simple" or mixed tumour. Seventy-five per cent. of all these occur in the parotid. They are really endotheliomata, developing from branchial rests. It is to be remembered that sooner or later the great majority of these tumours take on malignant growth—thus they are dangerous, and their treatment should be removal as early as possible.

Growths (Malignant).—In these growths the facial nerve is usually early involved, and there are symptoms of various obstruction in contradistinction to the innocent growths. For such growths the whole parotid gland has been frequently removed together with the lymph glands in the upper part of the neck—such an operation is obviously a formidable one, and in my opinion it should not be undertaken except in very early cases where the diagnosis has been confirmed on incision by an immediate microscope section. In all such cases, the prophylactic use of radium and X-rays is to be recommended often, and the same means are all that is left to us in the inoperable cases.

Salivary Fistulæ.—These are usually the result of injury. If they occur in the glands themselves, they usually close spontaneously, if not the use of the cautery will usually rapidly effect a cure. On the other hand, a fistula of the parotid duct on to the face has very little tendency to close spontaneously. Here the best treatment is not to waste time, but to slit up the duct freely into the cavity of the mouth and make an internal fistula out of it.

Ludwig's Angina, though hardly an infection of the salivary glands, is usually an acute cellulitis of the floor of the mouth, originating in the submaxillary lymph glands. Its causes are manifold—suffice to say that this condition may result from any septic wound in the mouth, pharynx and upper air-passages. By far the most frequent organism is some form of streptococcus, usually the streptococcus longus; the pneumococcus and the B. diphtheriæ are also frequently found. The dangers of what is described as a "collar-swelling" in the neck cannot be exaggerated, and the onset of acute œdema of the larynx has usually no definite relation to the amount or duration of the external swelling

—early incisions should be the invariable rule if there is any reason to fear this condition—it is far better to incise a collection of inflammatory glands than run any risk of leaving Ludwig's angina to pursue its course—a cultivation should be taken and an attempt made to procure a vaccine for future use.

Meanwhile the wounds should be left open. I have recently in this, and other septic conditions smeared the whole raw surface freely with "Iodex," and have had admirable results. It is obvious that skilled nursing should be at hand in all such cases, until the inflammatory symptoms are at an end, and that tracheotomy should be at once resorted to on the *very slightest* respiratory difficulty. At the risk of repetition it cannot be too strongly insisted on that there should not be any hesitation or delay in performing tracheotomy even though the difficulty in respiration seems but trivial. J. K. M.

DISEASES OF THE TONSILS

Removal of Tonsils

When from adequate reasons it is decided that the tonsils should be removed, it is axiomatic that the more completely this is carried out the better, if recurrence of symptoms is to be avoided. This does not necessarily mean that a severe dissecting operation is a *sine quâ non*. Though the old-fashioned operation of tonsillotomy by means of a *sharp* guillotine frequently failed to remove sufficient to prevent recurrence of symptoms, and rarely removed more than nine-tenths of the tonsil, it does not follow that operation with the guillotine alone should be regarded as obsolete, and that all tonsillectomies in future should include partial dissection; for it is abundantly proved that with a *slightly blunt* guillotine alone a complete extra-capsular excision of the entire tonsil can be frequently, and even usually, accomplished by an expert operator. In *buried tonsils with septic crypts*, and in tonsils where the pillars and plica are adherent, complete enucleation by a dissecting operation for freeing the pillars before applying the snare or the blunt guillotine or using the bistoury is usually essential.

The various methods of removal at our disposal may be summarised as follows—

1. With *sharp* guillotine plus external digital compression below the angle of the jaw carried out by the anæsthetist or by an assistant. This method is often inefficient.
2. Blunt guillotine plus external compression.
3. The foregoing combined with traction through the ring of the guillotine by the vulsellum.
4. Blunt guillotine plus internal digital compression at the anterior pillar of the fauces made by the operator in order to squeeze the large tonsil through the smaller ring; to this external compression can be added. This method, originated by Whillis, is the method of choice with a large number of experts at the present day. Sluder's method is somewhat similar. The shaft of the guillotine should be directed towards the tonsil from the angle of the mouth of the opposite side, and the ring of the instrument used as a raspatory to detach the gland from the posterior pillar and, with its capsule, from the tonsillar bed in a direction upwards and forwards, so as to bring it against the eminence on the lower jaw produced by the last molar tooth; the blade is then driven home. The only disadvantage in this method (Sluder's) is that the anterior pillar is usually slightly wounded, and Peters therefore prefers to make two cuts with the guillotine, the first a slight one to detach the tonsil from the anterior pillar; the cutting blade is then readjusted and the ring made to displace the tonsil further upwards and forwards before the second stroke, which removes the whole tonsil with its capsule, is carried out.
5. Blunt guillotine plus internal or external compression, or both plus vulsellum.
6. Snare, plus compression, plus vulsellum.
7. Dissection, *i. e.* instrumental separation of superior pole of the tonsil and of the adherent pillars, aided by traction with vulsellum, and followed by attempted complete enucleation with finger.
8. Dissection with the aid of dissector and vulsellum, as in the foregoing, followed by complete removal with a blunt guillotine; digital compression can be employed to supplement traction with the vulsellum. This is the operation favoured by many specialists (when dissection is indicated) as being almost bloodless in many instances. It is an operation which is only suitable for experienced and expert handicraftsmen, and has the disadvantage of requiring a fairly deep anæsthesia.
9. A snare can be substituted for the guillotine in the last method (No. 8).

When the tonsil, after any of the above operations, is still adherent at one spot and the instrument is "held," the finger is used as a separator and swept round the bed of the tonsil.

Of these operations, 2 and 4 are the favourite procedures, and by such simple means the majority of enlarged tonsils can be satisfactorily removed, provided a not too sharp guillotine of sufficiently small size be employed and the operator is reasonably expert, more especially in threading the tonsil into the instrument from the inferior pole.

Many experts, however, prefer to carry out tonsillectomy by means of a vulsellum and snare, and claim that there is less trauma and hæmorrhage.

For adherent and for buried tonsils a dissecting operation such as 8 or 9 should be resorted to in order to effect a complete excision

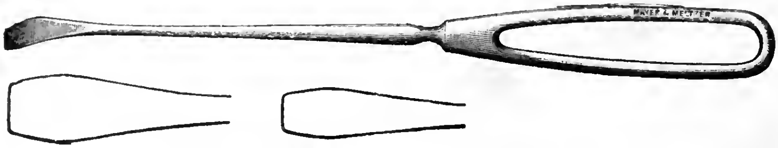


Fig. 1.—Dan McKenzie's Tonsil Dissector.

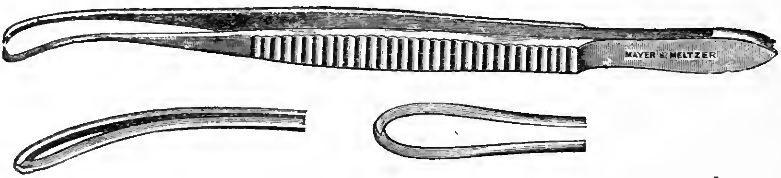


Fig 2 —Hope's Tonsil Forceps, which can be used either as a tenaculum or as a dissector.

of the tonsil along with its capsule. It must be remembered that there is often greater inflammatory reaction and increased liability to hæmorrhage after dissection operations,

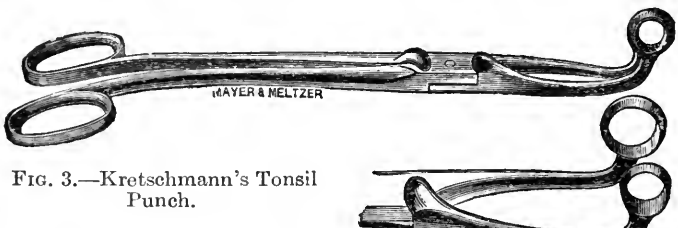


Fig. 3.—Kretschmann's Tonsil Punch.

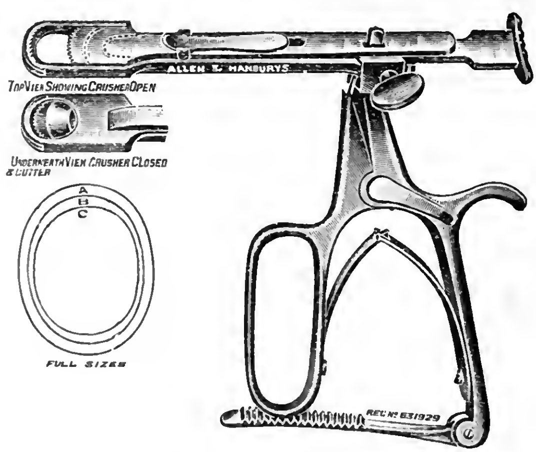


Fig. 4.—Elphick's Hæmastatic Guillotine.

and with the capsular barrier removed increased risk of infection of the adjacent lymphatics. There is much difference of opinion as to the employment of the knife or of a blunt dissector for detaching the pillars; the advantage of a blunt instrument is that it is also available for freeing the superior pole of the tonsil containing the *crypta magna* (tonsillar recess).

10. Removal of the parenchyma, leaving the capsule intact, by *morcellement*, accomplished either by digital scarification or by punch forceps, is mentioned only to be condemned if carried out as a complete operation, though partial *morcellement* with Kretschmann's punch is justifiable for the removal of small portions of tonsillar tissue left behind after other operative methods, especially after attempted enucleation by finger, or by dissection, in which the tonsils turn out to be very friable.

The position of the patient, whether sitting in a chair or lying in the extended position on a table, the choice of anæsthetic and the question of long or short anæsthesia, are points on which it is impossible to dogmatise in view of the divergent opinions and practice obtaining among experts. Open chloroform anæsthesia on a table or couch is essential in the case of slow or only moderately experienced operators, when any operation which includes dissection is about to be carried out.

As regards tonsillectomes, the modifications of McKenzie's guillotine still hold the field in this country, Hugh Jones's pattern and also Heath's being largely used. I sometimes employ a McKenzie guillotine with a lifting fork attached for buried tonsils. Ballinger's tonsillectome is much used in America, and after two years' experience with it I can recommend it as a very efficient one-handed instrument, though rather complicated for rapid cleansing in hospital practice. Elphick has recently modified Ballinger's instrument by strengthening the crushing blade and adding a sharp-edged blade to detach the tonsil from the crushed stump, thus securing hæmostasis.

W. H.

SPECIAL TOPICAL METHODS OF TREATMENT OF THE FAUCES AND PHARYNX

Whilst general medical treatment alone suffices in some diseases of these regions, and is indicated

in association with local measures, in many others the modern tendency is in the direction of increased refinement in and the wider application of local measures. The methods at our disposal include the employment of—

1. Watery fluids as gargles, sprays and douches.
2. Oily fluids as sprays.
3. Pigments.
4. Lozenges and pastilles.
5. Insufflation of powders.
6. Inhalations either in the cold and dry, or in the hot or vaporised, form.
7. The application of heat and cold.
8. Cauterising agents.
9. Electrical methods, including faradism, galvanism, the sinusoidal or wave current, ionisation, diathermy and galvano-cauterisation.
10. Ray treatment, either by the Roentgen rays or by radio-active substances such as radium salts and thorium.

Watery Fluids

Gargles.—Cleansing, astringent, stimulating and anodyne solutions are largely prescribed. Gargling, however, is not a very efficient method for obtaining the maximum local application of any therapeutic agent to the pharynx, and is oftener than not on a par with using a mouth-wash, a useful enough measure of course as such. In acute conditions it is painful and often impossible to gargle, and in subacute inflammations the solution rarely passes beyond the fauces. Gargling, however, with astringents, *e. g.* solutions of alum and even with cold water in chronic relaxed and paretic conditions of the palate, is often of service when the patient has acquired the knack of carrying it out efficiently.

Coarse Sprays and Douches.—Alkaline lotions for clearing the fauces and pharynx of thick mucus or adherent false membrane and sloughs is best carried out by a coarse atomiser, the nozzle of which is movable so that the stream can be applied in various directions when the nozzle is inserted well into the throat; the tongue may require depression. A stronger impact can be obtained by using a syringe or syphon douche with a suitable nozzle; this method is especially indicated in the naso-pharynx, but is also useful elsewhere when the atomiser proves inefficient.

The following watery solutions can be used either as sprays, douches or gargles—

Detergent and Alkaline.

℞ Pot. Chlorat. (vel. Sodii Chloridi vel. Ammon. Chloridi) ℥ ss
Boracis ℥ ss
Sod. Bicarb. ℥ ss
Sacch. Alb. ℥ i

One dr. to be dissolved in half a tumbler of cold water. Warm water can be used for gargling and douching.

(This is the well-known "Pulv. Chlor. Co." of the Central London Throat and Ear Hospital Pharmacopœia.)

℞ Sod. Bicarb. gr. xv
Boracis gr. xv
Acidi Carbolici gr. iv
Glycerini ♏ xlv
Aq. ad ℥ i.

(This is the Nebula Alkalina of the Throat Hospital Pharmacopœia.)

Astringent.—The following quantities represent the dose to an ounce of water in each case—

Alum gr. v–xv
Sulphate of copper gr. v
Chloride of zinc gr. x–xx
Sulphate of zinc gr. x–xx
Tannic acid gr. v–x.

Lotio Krameriæ Co.

℞ Tr. Krameriæ ♏ x
Tr. Myrrh ♏ x
Tr. Lavand. Co. ♏ v
Glycerini Borici ʒ i
Aq. ad ℥ i.

An astringent and sedative mouth-wash and gargle.

Lotio Boracis Co.

℞ Boracis gr. xxv
Tr. Myrrh ♏ xxv
Glycerini ♏ xxv
Aq. ad ℥ i.

Sedative.—

Chlorate of Potash gr. x–xx Borax gr. x–xx Glycothymoline ʒ i–iii Listerine ʒ i–iii Dilute Hydrocyanic Acid ♏ iii	to the ounce of water in each case.

The last is useful in cough of tuberculosis—only about ½ dr. to be used at a time as a spray.

℞ Lotio Nigra ℥ ss
Pot. Chloratis gr. x
Aq. ad ℥ i.

Useful as a sedative and antiseptic mouth-wash and gargle in syphilis.

Antiseptic Mouth-washes, Gargles and Douches.

Resorcin gr. x–xx Permanganate of potash gr. ¼–i Sanitas ♏ xxx Biniodide of mercury gr. ⅛ Perchloride of mercury gr. ss Salicylate of soda gr. x	to the ounce of water in each case.

℞ Sodii Benzoatis ʒ ii
Resorcini ʒ ss
Phenozoni ʒ i
Glycerini ad ℥ viii.

A teaspoonful in half a tumbler of tepid water. An antiseptic and soothing gargle or douche.

℞ Acidi Salicylici ʒ i
Sodii Chloridi ʒ x
Sodii Bicarbonatis ℥ ii ss.

Half a teaspoonful in a tumbler of tepid water; in septic and rheumatic tonsillitis as a douche.

Resolvent.—To facilitate the detachment of false membrane and sloughs any of the following sprays may prove useful—

Liquor Calcis.
Lactic acid ʒ i–ii to the ounce of water.
Salicylate of soda gr. xx to the ounce of water.
Papain gr. x–xx to the ounce of water.

Oily Solutions

These can be used either by means of a special atomiser or with a brush.

℞ Menthol gr. x ad gr. xx
Thymol gr. i ad gr. v
Eucalyptol ♏ i ad ♏ v
Parolein ad ℥ i.

This strong menthol spray should only be employed as a stimulant and sedative in atrophic conditions. In sub-acute tonsillitis and pharyngitis 2 to 5 gr. of menthol to the ounce is usually of sufficient strength.

℞ Camphor-menthol gr. x
Parolein ℥ i.

A sedative in acute inflammation of the fauces and pharynx.

℞ Menthol gr. v
Cocaine gr. xx
Ac. Oleic ♏ xv
Parolein ad ℥ i.

Sedative.

Pigments

Guaiacol (pure).

This should be applied only after cocainisation by the practitioner himself. Occasionally useful for aborting an acute tonsillitis.

℞ Guaiacol ʒ ii
Glycerinum ad ℥ i.

This can be applied by the patient to the tonsils thrice at intervals of two hours to endeavour to abort an acute tonsillitis with lacunar exudations (so-called follicular tonsillitis).

The following is the formula of the well-known Mandl's solution, which, however, is not so much in vogue as formerly.

℞ Iodi Puri gr. v ad gr. x
Pot. Iodidi gr. xx vel. q. s.
Ol. Menth. Pip. ♏ v
Glycerini ℥ i.

Stimulant and antiseptic in atrophic pharyngitis; it is also used to cut short sloughing and to stimulate healing after tonsillectomy in debilitated subjects. Its employment for subacute and chronic hypertrophic pharyngitis in voice users has been largely given up in favour of alkaline sprays and douches, and the milder application of atomised menthol.

Deliquesced Chromic Acid.—Applied pure as a caustic and stimulant in syphilitic ulcers. Since the introduction of salvarsan the use of this and other caustics has been largely abandoned.

Lactic Acid.—Applied pure as a caustic to ulcers. Twenty to fifty per cent. solutions were formerly much used in diphtheria and in tuberculosis; since the introduction of therapeutic inoculation methods, however, such applications are rarely made.

Boroglyceride.—Applied either pure or diluted with an equal quantity of glycerine in septic ulcerative conditions.

℞ Resorcin ʒ i ss
Glycerini Boracis ℥ i.

Antiseptic and Astringent.

℞ Chloride of zinc gr. xv–xxx to the ounce of water
Sulphate of zinc ʒ i to the ounce of water.

Local Anæsthetics

℞ Cocainæ Hydrochloridi gr. xxiv ad xcvi
Acidi Salicylici gr. ss
Aq. Destill. ad ℥ i.

These solutions, varying from 5 to 20 per cent., should be applied by the surgeon with a brush to produce local anodyne action in painful conditions or for local anæsthetic purposes in endoscopic and surgical measures. Twenty-five gr. of suprarenal extract (Merck) can be added if a marked ischæmic effect is desired. A smaller quantity of one of the numerous forms of suprarenal gland extract or its synthetic equivalent is useful for mitigating the toxic effect of cocaine by limiting its absorption into the general circulation.

℞ Cocainæ Hydrochloridi gr. xx vel. q. s.
Phenozoni gr. xl
Liq. Thymol Alcoholici ♏ ii
Aq. Destill. ad. ℥ i.

The phenazone is said to increase the anæsthetic action and the thymol solution tends to preserve the solution, like the salicylic acid in the preceding formula.

Eucaine can be substituted for cocaine in the above two formulæ, but it is not so readily soluble in water, so that it is only suitable for 5 to 8 per cent solutions.

Submucous Injections

Ampoules containing a 2 per cent. solution of novocaine, together with suprarenin (synthetic), are sold, and are useful for minor operations, *e. g.*

for injecting the pillars of the tonsils previous to tonsillectomy without a general anæsthetic. Synthetic suprarenin possesses the advantage over the animal extract in that it can be boiled if necessary. The composition of an ampoule is as follows—

℞ Novocainæ gm. 0·1
Suprarenin Boratis gm. 0·00045
Sodii Chloridi gm. 0·045
Aq. Destill. ad c.c. v.

Pastes

The only form of paste included in the Throat Hospital Pharmacopœia is Pasta Acidi Tannici, which is made by mixing together tannic acid 3 parts, and gallic acid 1 part, and adding a few drops of water, and kneading till a firm mass is formed. A portion about the size of a marble is then held against the bleeding surface of the tonsil to arrest severe hæmorrhage after tonsillotomy. Lennox Browne recommended the sipping of a thick saturated solution in which ½ oz. of the above powder is dissolved in 1 oz. of water.

A thick paste of bismuth oxychloride to which 5 to 10 gr. or more of chloretone or of orthoform has been added to 1 oz. of paste is useful in painful ulcerating conditions in the throat and gullet, as when the mass is swallowed much of it tends to stick for a considerable time on the ulcerated areas. The coating of bismuth is sedative in itself apart from the added analgesic powders.

Lozenges, Compressed Tablets and Pastilles

The lozenges and pastilles hereafter mentioned are chiefly of the composition set forth in the well-known Throat Hospital Pharmacopœia. These agents are admirably adapted for exercising a prolonged influence on the mouth, fauces and pharynx. Some of them, unfortunately, upset the appetite and digestion if taken with frequency. This applies not only to those containing morphia, but is a marked characteristic of the slowly dissolving lozenges and compressed tablets containing chlorate of potash, so largely prescribed. For rapid action pastilles made up with a glyco-gelatine base are to be preferred. Rhatany, kino and tannin are chemically incompatible with gelatin. Lozenges made up with fruit paste also produce an immediate local effect, and this base can be used for most lozenges, those containing carbolic acid being exceptions. The hard base of the officinal lozenge and the compressed tablet form, therefore, are, generally speaking, suitable only when a constitutional action is aimed at together with a prolonged local effect, *e. g.* the morphia and ipecacuanha lozenges and the codeine lozenges. Bromide of potassium, chloride of ammonium, borax and chlorate of potash are largely prescribed as compressed tablets as cheaper and more convenient for carrying about than when a fruit base is employed.

Lozenges. — Trochisci Sedativi (containing $\frac{1}{10}$ gr. of extract of opium in each); Trochisci Cocainæ ($\frac{1}{10}$ gr. of cocaine); Trochisci Acidi Benzoin. Co. (containing hydrochloride of cocaine and codeine); Trochisci Morphinæ cum Ipecacuanha and Trochisci Orthoformi, all have an *analgesic* action.

Trochisci Boracis is merely *sedative*, and Trochisci Acidi Carbolici is antiseptic and stimulant as well as sedative in action. The following have a *stimulant* effect: Trochisci Acidi Benzoici, Trochisci Ammonii Chloridi, Trochisci Ammonii Chloridi Co. (containing also cubebs and chlorate of potash), Trochisci Cubebæ and Trochisci Potassii Chloratis.

For relaxed conditions the following *astringents* are largely used: Trochisci Krameriæ, Trochisci Krameriæ Co. (containing cocaine), Trochisci Catechu. Trochisci Acidi Tannici is rather too astringent for prolonged employment and liable to upset the digestion.

Trochisci Guaiaci is said to be antiphlogistic and is also given in rheumatic and gouty subjects.

A number of proprietary lozenges containing either menthol or formic aldehyde are largely consumed by the public; the former are sedative and stimulant and the latter antiseptic, and they appear to be often of much service.

The well-known Brompton Hospital Lozenge owes its sedative action to liquorice and anise seed, and the ordinary "delectable lozenge" to tolu. Marshmallow pastilles are merely demulcent; they serve to keep children quiet after tonsillectomy; there is often difficulty, however, in getting them fresh, and they are expensive.

Pastilles and lozenges cause less disturbance of appetite and of digestion when taken after food, but when an analgesic effect for the relief of dysphagia is aimed at they should be used a quarter of an hour before each meal.

In conclusion it is well to bear in mind that the most frequently prescribed lozenges, viz. the chlorate of potash and the tannic acid, are not suitable for prolonged use, and are perhaps best avoided in many patients: that nothing much can be expected from antiseptic lozenges which are necessarily weak and when dissolved in the saliva pass into the gullet without reaching the crypts and other regions harbouring pathogenic microbes: that they are most useful in sedative form for relieving cough and irritability and that even then such a valuable lozenge as that containing morphia and ipecacuanha probably owes its efficacy as much to its constitutional as to its local action. Even the astringent and the stimulating forms which are often most

effectual in subacute and chronic conditions may upset the appetite and digestion if taken too frequently and for long. Those containing cocaine or morphia must be given with special caution even although the dose is so small.

Pastilles.—The following pastilles (Throat Hosp. Phar.) are made up with a glyco-gelatin base—

Pastillus Bismuthi (sedative).
Pastillus Bismuthi et Morphinæ (sedative).
Pastillus Cocainæ ($\frac{1}{10}$ gr.) (sedative).
Pastillus Menthol ($\frac{1}{6}$ gr.) (sedative).
Pastillus Ammonii Chloridi (stimulant).

Powders for Insufflation

Powders are most conveniently applied by means of special insufflators, a straight nozzle being employed in the fauces and in the pharynx and an angular one for the naso-pharynx and for the deeper regions of the pharynx.

Analgesic. For the relief of painful dysphagia.—The following can be insufflated separately or together—

Chloretone gr. v–x
Anæsthesin gr. v–x
Orthoform gr. v–x.

The latter is useful in ulcerative conditions only.

℞ Morphinæ Hydrochloridi
Sacch. Lactis } (āā gr. $\frac{1}{4}$ ad $\frac{1}{2}$
Acaciæ Gummi gr. i.

In the painful dysphagia of tuberculosis of the laryngo-pharynx this sometimes gives relief for many hours.

Analgesic and Antiseptic.

℞ Orthoformi gr. v
Iodoformi gr. v
Menthol gr. ss.

In cancerous and other ulcers.

℞ Cocainæ Hydrochloridi gr. x
Morphinæ Hydrochloridi gr. iss
Menthol gr. x
Iodoformi ʒ ii
Acidi Borici ʒ ii.

Five grains at each insufflation in painful dysphagia.

Inhalations

Cold dry inhalations are not nearly so much used in inflammatory conditions in the pharynx as in the larynx. The same remark applies in a lesser degree to steam inhalations though they are sometimes found comforting in acute inflammations in the region of the fauces. For formulæ the reader is referred to the section on *Laryngeal Therapeutics*.

The Application of Heat and Cold

Heat.—The simpler methods of applying heat externally in the region below the angle of the jaw in acute tonsillitis and pharyngitis are so well known as scarcely to need enumeration, they include—

(1) The warmed comforter or small shawl.
(2) Cotton-wool or flannel, or spongiopiline, heated before a fire or in an oven, and kept in position with the hand or retained by a flannel bandage.
(3) Hot compresses and poultices.
(4) An india-rubber hot-water bottle or pillow.

Special apparatus include—

(5) Leiter's coil of leaden tubes with a continuous stream of hot water from a receptacle. The more modern rubber coil incorporated in a flat pad, and attached to a spirit-lamp apparatus, has the disadvantage of requiring skilled attention.
(6) The Thermos flask.
(7) The electric poultice, which has the advantage over the rubber hot-water pillow in that continuous heat can be obtained by connecting the apparatus with a wall-plug. By a special arrangement in the newest patterns the degree of heat required can be exactly regulated.

Internally, heat can be applied in the form of hot steam inhalations of benzoin, creolin or similar preparations. Hot mouth-washes appear to be of some use at times in acute inflammations of the fauces, especially in those cases where the drinking of hot tea and other drinks gives relief, but gargling is not usually well borne in acute disease.

Cold.—Although the sucking of ice is frequently advised for acute sore throat, it is to be doubted if it is often of any service for that purpose; on the other hand as a hæmostatic after operations it is frequently most valuable.

Leiter's continuous coil for the external application of cold was advocated as a routine measure in acute inflammations of the throat by Lennox Browne, but most practitioners rely on the hot coil rather than the cold, and the same applies to the ice-bag.

Cauterising Agents

The use of caustics either pure or in strong or in weak solutions was in former times almost a routine measure in most inflammatory lesions, whether acute, subacute or chronic, in the fauces and pharynx, whereas to-day many experienced specialists scarcely ever apply them; and on the exceptional occasions when they do have recourse to a destructive agent they usually rely on the electric cautery, which can be applied with greater surface precision than any solution, and any desired depth of

penetration can be effected. (See sections on *Pigments* and on *Electrical Methods*.)

Paquelin's cautery and the galvano-cautery snare is of service for the palliative removal of portions of malignant growths blocking the fauces and pharynx, and thereby interfering with deglutition, articulation and even respiration.

Electrical Methods

Faradism and Galvanism.—There is no wide scope for the employment of electrical currents in the fauces and pharynx. In paralysis of the constrictors of central origin electricity is not of much value. In obstinate *peripheral nerve paralysis* and paresis of the palate following diphtheria and influenza, faradism should be employed as long as there is any faradic reaction present; when the latter is lost galvanism can be applied either internally or externally. In *paretic palate* resulting from prolonged nasal catarrh the lesion is not a nerve one, but probably myopathic in some degree, and the application of the interrupted, *i. e.* faradic, current probably has an action of the nature of massage, and is not superior to vibratory massage. In *clonic spasms* of the palate and pharynx, faradic and galvanic currents are of doubtful service, but the sinusoidal current has been advocated in some quarters, as has also high frequency. In functional paresis of the fauces and pharynx with dysphagia, faradism sometimes works wonders, the element of suggestion no doubt having some share in the result in many cases.

Ionisation and Electrolysis.—These methods have rarely been used in the pharynx. Ionisation is too cumbrous a method to employ for the stimulation of indolent ulcers where caustic methods are equally useful; and though it has been claimed that electrolysis has occasionally been successful in bringing about the almost total disappearance of growths of moderate malignancy,. *e. g.* some endotheliomas and sarcomas, and Matthey of New York has attained some degree of success with zinc-mercury electrodes in carcinoma, yet the results are neither numerous enough nor striking enough to warrant recourse to them in inoperable cases of malignant disease in view of the fact of the more effective results of other methods, *e. g.* by radium and by surgical diathermy.

The Galvano-Cautery.—This is undoubtedly a convenient agent for producing destructive cauterisation when redundant tissue has to be removed, for producing fibrosis in tuberculous lesions, for the stimulation of indolent ulcers and for reduction of hyperæsthesia and paræsthesia by destroying temporarily the nerve-endings. The method is far less resorted to than formerly, when it was carried out as a routine measure though in a haphazard way in almost every case with chronic trouble in the throat. At the present day many experts rarely find occasion to employ this or any other method of cauterisation in the fauces and pharynx.

It is a very slow, frequently painful and often inefficient procedure for the reduction of enlarged tonsils. In what is known as granular pharyngitis, the projecting islands of hyperplastic lymphoid tissue are rarely the cause of the paræsthesia and other symptoms complained of, and these symptoms are rarely relieved by cauterising the so-called granules. The same may be said of prominent veins at the base of the tongue, though in this region the removal by the cautery point or with electric snare of redundant lymphoid tissue (lingual tonsil) in contact with an irritable epiglottis is sometimes useful in pharyngeal paræsthesia with cough. The cautery snare causes much more reaction than a pair of sharp scissors in uvulotomy. In angiomatous conditions and in small multiple papillomata the galvanic cautery is indicated when radium treatment is not available.

As regards the technique of its employment the same methods and precautions are necessary as in nasal electric cauterisation (*q. v.*).

Diathermy.—The production of aseptic necrosis in large inoperable tumours of the pharynx and exceptionally for the reduction of very large tonsils can be accomplished by the employment of a special form of high-frequency apparatus by which deep coagulation and cauterisation is effected. The reader is referred to the special article on this subject (*q. v.*).

Fulguration.—This form of high-frequency current is advocated by Dr. Keating Hart of Paris. The sparking is applied from five to ten minutes according as the malignant growth is of moderate size or of considerable dimensions. It does not, like the Diathermic and Desiccation methods, produce destruction of the growth, but is said to affect the nutrition of the tissues and render the soil less fertile for the proliferation of the cancer cells; whether cancer growth can effectually be inhibited and atrophied to the extent claimed by the originator of this comparatively simple method remains to be confirmed.

Desiccation by Static Electricity of High Tension.—By this method the spark used is not hot enough to carbonise the malignant tissues, but only sufficient to cause rapid dehydration, thereby rupturing the cell-capsules and converting the area treated into a dry mass. Clark of Philadelphia claims a wide application and a considerable measure of success for this procedure in the reduction of innocent and malignant growths in the nose, pharynx and elsewhere. He even employs it for the reduction of hypertrophies such as enlarged tonsils and adenoids. In cancerous growths

whilst accessible superficial lesions can be desiccated the glands and deeper extensions are best dealt with either by the X-rays or with radium.

Whether these claims on behalf of desiccative methods will be substantiated by others remains to be seen.

The X-Rays

Since the introduction of treatment by radium the older method of Roentgen radiotherapy has not been much used in the fauces and pharynx; and when employed the application is usually made from the outside towards the angle of the jaw and side of the neck for large *malignant growths* of the fauces and base of the tongue, for invasions from the larynx, for cancers of the deep pharynx, and more especially for the glandular extensions in the neck. It has also been applied through the mouth, in America, for growths in the region of the faucial ring.

Quite recently Steuart of Birmingham has claimed some measure of success from the use of X-rays in the partial *reduction of enlarged tonsils* and also adenoids in cases where operation is either undesirable or undesired. It is too soon to say whether the method is worth the trouble involved in its employment and is of any use in indurated large tonsils of long standing. The following is Steuart's summary of the technique: "A hard tube having a penetration of nine Wehnelt units was used, the rays were filtered and not more than a half Sabouraud dose was allowed to pass through any given area of skin. The rays were applied laterally, the anticathode of the tube being above and behind the angle of the jaw, so that the rays encountered the minimum resistance in reaching the tonsil; the head was so placed that the rays swept in front of the vertebral column and the posterior pharyngeal wall. After a dose had been given on one side the head was turned and a similar treatment given on the other side.

"All measurement was done with a pastille lying on the skin. With restless children it is useless to adopt Sabouraud's plan of having the pastille half-way between the anticathode and the irradiated area.

"The tube was placed at a greater distance from the patient than is usual in order to obtain approximate equality of intensity of radiation throughout the pharynx.

"The interval between the doses was usually three weeks, but under no circumstances was a larger dose than a half Sabouraud given."

Screened Radium Salts and Radium Emanation

The mode of action, possibilities and limitations of the radio-active rays of radium in innocent and malignant tumours in general, is dealt with in a separate article in this work. The method is now extensively employed in cancerous disease in the faucial region, the pharynx, the larynx and the gullet. The remedy is a very uncertain one, but very substantial palliative results, sometimes amounting to temporary disappearance of naked eye evidence of disease, have been recorded in an encouraging number of instances where, though operation was either contra-indicated or rejected, yet the growth was not too advanced. It is very occasionally useful in so reducing a cancerous condition considered inoperable as to permit of subsequent surgical removal with success. As a rule, however, the cases one is asked to deal with are not only inoperable, but so far advanced

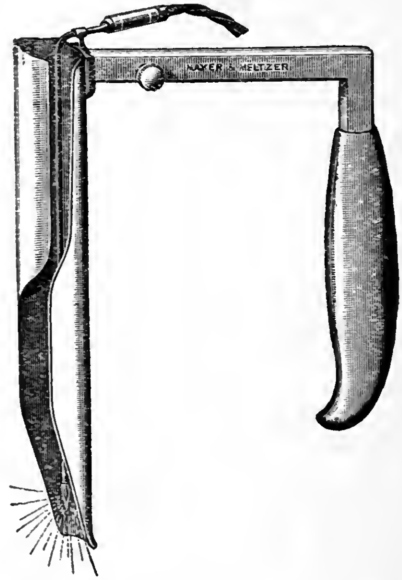


Fig. 5.—Hill's direct Pharyngoscope and Laryngoscope, with distal lamp, for inserting the radium apparatus in pharyngo-laryngeal malignant diseases.

as to be untreatable, so that little can be hoped for beyond such a reduction of the growth as will palliate the more distressing symptoms, such as mechanical difficulties to swallowing and respiration, painful ulceration and excessive secretion. So-called recurrences, that is, small areas of growth which make their appearance early after an unavoidably imperfect removal by operation, are always worth dealing with by radium therapy, and gratifying palliative results and even temporary apparent local cures are occasionally obtained. Of malignant growths, endotheliomas and other forms of sarcomas react in the throat (as in the gullet and elsewhere) more readily to radium rays than do true carcinomas; squamous epitheliomas seem to be least favourably influenced of any, but I have seen at least six such cases, four

being in the deep or post-cricoidal pharynx, which have reacted quickly and very markedly to repeated applications of radium, with consequent

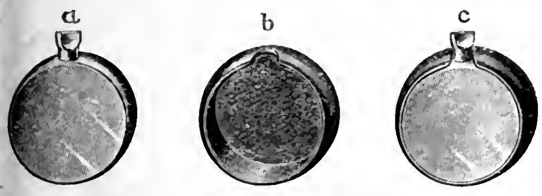


FIG. 6.—Circular box which, when charged with emanation, is sealed at *a*; *b* is an extra screen to protect healthy tissues, which fits on *a* as in *c*.

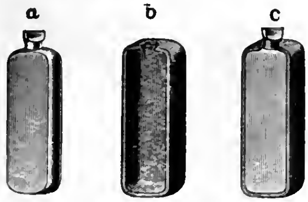


FIG. 7.—*a* is a metal box for radium emanation, with walls 1 to 2 mm. thick; *b* is an additional screen to fit over *a* as in *c*. to protect the adjacent healthy mucosa. This form of apparatus is employed in post-cricoid cancer.

symptomatic relief for periods varying from six to eighteen months. In these cases the glandular and other extensions led to the fatal issue rather than the primary throat lesion. There are some recorded instances of sarcoma limited to the tonsil having apparently disappeared altogether. A small tube should be inserted into the growth and an emanation box applied to the faucial surface. Such cases, however, are more quickly and certainly dealt with by operation, radium therapy generally speaking being reserved for those in which operation is either contra-indicated or declined. Radiation can, however, be usefully employed after operation.

In my own practice I have usually employed one or more tubes containing 100 mg. of radium bromide (or its equivalent in other salts of radium) or tubes or caskets containing the emanation equivalent.

The drawback to the use of emanation is that it loses its radio-activity, the fall being rather rapid to begin with, so it is reduced to half strength in something under four days. As the curve is, however, definitely known, one is able to order approximately a dose equivalent to say 100 mg. of radium bromide for a twelve-hour application, the radio-activity being higher than that amount to begin with, but averaging out fairly correctly. On the other hand, against this disadvantage compared with the use of tubes of pure radium salts, where there is only a negligible variation in strength, it is at times a great convenience to be able to get a box or casket built to a size and shape suitable for each individual case, and the emanation is then equally distributed throughout the containing chamber, whereas with tubes only partially filled with radium, as many are, the distribution of the radium salt in the tube is affected by position.

In my own practice I have almost entirely worked in the throat and gullet in conjunction with Finzi, using his radium tubes enclosed in platinum screens; which latter have the advantage of being more efficient than either lead, silver or German silver of the same degree of thickness; this thickness in Finzi's screens varying from $1\frac{1}{2}$ to $2\frac{1}{2}$ mm. It is alleged that there is a drawback to platinum as a screening agent in that it gives off a more powerful secondary radiation than either lead, silver or German silver, but as all screens are enclosed in rubber to counteract this secondary effect it is probable that the objection to the use of platinum is more theoretical than practical.

In using tubular screens an outer screen with a window on one side is useful in the deep pharynx and in the gullet when the lesion has not yet become annular, but is limited to a

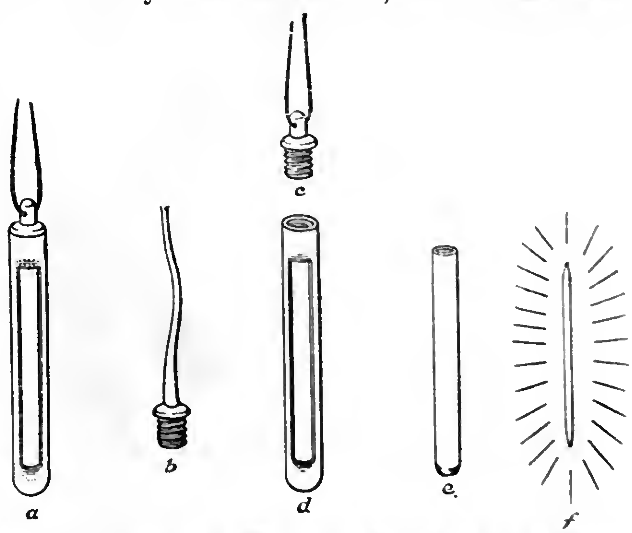


FIG. 8.—*f* = capillary glass tube containing radium emanation which is enclosed in the metal tube *e*, whose walls are 1 mm. thick; this again can be enclosed in an additional screen, *d*, with a window which is arranged adjacent to the growth; the whole is secured by a screw cap, *c*, which has a string through it; or a cap *b* with a long flexible silver style attached can be substituted more especially for œsophageal cancer.

certain part of the wall, *e. g.* to the back of the cricoid plate or to the pyriform fossa; the thinner part of the screen, *i. e.* the region of the window, is then accurately placed against the

cancerous area under direct vision through the endoscope and the non-invaded areas are protected by the additional thickness of metal; and further protection can be obtained by interposing an additional layer of rubber or lint. In the fauces and mesopharynx a roll of lint tied on to the surface of the tube which is away from the growth forms quite an efficient screen by distance for the protection, for example, of the healthy uvula and palate or for the epiglottis. Where an emanation box is employed an accurately fitting cap of lead or other metal can be used as an additional screen to protect healthy parts over and above the 2 mm. thickness of the box, which is only separated from the surface to be treated by rubber 1 mm. thick.

Having fitted up a suitable apparatus for any special case, either one tube, or two tubes abreast, or an emanation box of suitable size and shape with correct screening arrangements, the next thing to be considered is how to retain it accurately in contact with a desired area. In the case of the deep pharynx this is quite simple, as the radium apparatus is tied on to the middle third of a small œsophageal bougie, one end of which is passed into the gullet to anchor, so to speak, the whole apparatus below, and the proximal end is clamped to the teeth or to a denture. In the region of the fauces and lateral wall of the mesopharynx the ordinary gum elastic bougie is unsuitable for retaining the radium tubes or an emanation box in accurate contact with a diseased area, but I have had no difficulty since I adopted the plan of tying the radium apparatus to my styletted œsophageal tube (see p. 280), which is much more comfortable than tonsil pressure forceps. My apparatus consists of a red rubber tube 5 mm. in diameter, through the lumen of which passes a flexible silver style attached to a vulcanite terminal. This tube can be moulded to any required curves or angles after the distal extremity has been anchored in the œsophagus, and the attached radium apparatus can thus be accurately approximated to the growth in any desired position. This arrangement can often be retained *in situ* for twelve hours on a stretch, the patient being under morphia and atropine; but if there is much cough and irritation, or much septic secretion, it is better to be content with a six hours' application repeated at an interval of a day, or two or three applications of four hours each. These time-doses apply also to the pharynx, when 100 mg. of radium bromide or the emanation equivalent is employed with a 2 or $2\frac{1}{2}$ mm. metal screen encased in rubber in contact with the growth. It is best to apply two or three tubes arranged abreast for larger growths, rather than make two or three applications of twelve hours each on different areas. A word of caution is necessary in reference to cancers involving the laryngo-pharyngeal margin, *e. g.* the ary-epiglottidean folds and arytenoids; here the pressure of the apparatus alone may cause greatly increased tumefaction in the course of three or four hours leading to respiratory obstruction and retention of secretion. Moreover, as swallowing during the application is not always efficient, septic secretion may pass into and infect the air passages, when a large cancerous mass is complicated by a good deal of foul discharge. Moreover, in some cases the presence of the apparatus induces a good deal of salivation unless this is kept under control by morphia and atropine injections. I know of one case in which laryngeal stenosis necessitating tracheotomy followed the employment of radium for pharyngo-laryngeal carcinoma, and in a case in which I made the application myself for such a lesion, the patient died a few days later from septic pneumonia, which I strongly suspect was due to septic discharges passing into the air passages instead of being swallowed. In post-cricoidal carcinoma there is no passage left for swallowing when the apparatus is in position, and expectoration has to be relied on to get rid of excessive secretion, but it is only in lesions extending to the laryngeal vestibule that I have known serious complications occur. In treating the fauces the patient can swallow saliva fairly easily provided a small styletted tube is employed so that there is little danger of either laryngeal stenosis or the inhalation of septic discharges. In some intolerant patients and in those without sufficient fortitude, the apparatus has to be placed in position under general anæsthesia in deep pharyngeal cancers, but in my practice an injection of morphia and scopolamine, together with the local application of cocaine applied by the brush, has in the majority of cases been sufficient. When the disease is in the region of the lateral walls or laryngeal orifice, *i. e.* low down in the mesopharynx, and also when in the deep pharynx, the apparatus is best inserted through a large-sized open direct pharyngoscope (see p. 266). Great care must be taken to ensure that the apparatus is in its correct position, and the flexible silver wire of the tube must be forthwith bent in such a way as efficiently to retain it there. Frequent inspections, if necessary with the throat mirror, are of course advisable in cases where there is any tendency to coughing or vomiting, which might slightly shift the apparatus. Some patients suffer a good deal from thirst when much morphia and atropine has to be administered, and sucking ice often makes them more comfortable.

It is permissible in the case of very large growths to make two or three incisions into the tumour and bury two or three tubes in it. In

a patient under my care two years ago, no less than four tubes were inserted into a large naso-pharyngeal sarcoma which filled the naso-pharynx and pushed the soft palate forwards within an inch of the teeth. Before treatment he swallowed with difficulty, could only breathe through a tracheotomy tube, and was extremely deaf. A tube was inserted into the growth through each nostril, and two others through the mouth. At the end of a fortnight the naso-pharynx was comparatively clear, he could hear perfectly with one ear, and fairly well with the other, swallowing was normal, and the tracheotomy tube was dispensed with. Further treatment of the bone invasion was disappointing.

As cases referred for radium treatment are usually advanced and inoperable, the glands in the vicinity are frequently involved, and these must be treated either immediately after or before the primary lesion. The technique is necessarily different where healthy skin and subcutaneous tissues intervene, and this matter is fully dealt with in the special section on Radium Therapy (*q. v.*).

If the growth gives an unequivocal response to the treatment this will usually be evident in from one to three or four weeks, and the question of repeating the dose will then arise. Finzi follows the practice of Dominici of waiting till the reaction is well over, and not making a second application till about six weeks after the first. This course is also adopted at the Radium Institute, and the method, formerly so general in France, of giving large weight-doses and small time-doses frequently repeated with short intervals is not usually adopted in this country to-day, though it should be mentioned that Guisez's rather successful early observations with radium in cancer of the pharynx and gullet were carried out by the older and more tedious method.

To suggest the employment of radium for the removal of *innocent new growths* may seem on a par with breaking a fly on a wheel, but there are two conditions of the pharynx—of great rarity, it is true—in which radium treatment is likely to be more convenient and efficient than any other, viz. in extensive spreading lesions of an angiomatous character, and in recurrent multiple papillomata. Radium rays usually act well in contracting vascular growths in any region, and it has been shown by Abbé that it is equally efficacious in dealing with multiple papillomata of the larynx which tend to recur after repeated operation. Exceptionally, the condition spreads from the larynx to the pharynx and gullet, resisting all treatment, and Robinson has recorded a death in a case in which this extension took place. It would be worth while to give radium treatment a trial in such a case. Abbé employs only short exposures of half an hour, which can be repeated, and he uses a thin screen only.

Therapeutic Inoculation

Seeing that the throat is so commonly affected by septic inflammations, by diphtheria and by tuberculosis, it follows that treatment by serums, vaccines and antitoxins is of very wide and frequent application in this region. The subject, however, is fully discussed under the special section devoted to these methods generally, which renders it unnecessary to go over the same ground again; but attention may be called to the recently introduced practice of *local serum-therapy* more especially in diphtheritic lesions in the throat. A special serum which is possessed both of antitoxic and bactericidal properties is applied locally to the patches as an adjunct to the usual routine injection of diphtheria antitoxin. Such a serum is obtained by injecting an already immunised horse with living diphtheria bacilli. Horse serum already rendered antitoxic then contains antibodies which neutralise and destroy the bacillus itself. Behring long since insisted on the value of local applications to the lesions and does so again in his latest work. Leroy, referring to this adjuvant treatment, states that several months' experience in his diphtheria wards had convinced him that local applications of serum modifies the course of the attack. It has also been recommended as a prophylactic in scarlatinal and other lesions of the throat which tend to be complicated by diphtheria more especially during epidemics. It has likewise been employed with a view to sterilising the mouth and throat of "carriers." Whether the claims for this topical method made by Leroy, Dutour and others is destined to be unequivocally established in diphtheria and in other microbic diseases in the throat remains to be seen. The modern practice here in diphtheria at all events has been in the direction of avoiding local applications in order to disturb as little as possible patients who are so liable to fatal heart failure. W. H.

THE TREATMENT OF THE COMMONER DISEASES OF THE FAUCES AND PHARYNX

Acute Tonsillitis and Pharyngitis.—The acutely inflamed tonsil may be very enlarged (*Parenchymatous Tonsillitis*)—or the outstanding feature may be the presence of scattered croupous exudation from the mouths of the crypts, with or without marked enlargement (*Lacunar*, otherwise called *follicular* or *Discrete Exudative Tonsillitis*)—or the tonsillar surface may present a large patch of false membrane which is usually due to the Klebs-Lœffler

bacillus (*True Diphtheritic Tonsillitis*)—or membranous tonsillitis may exceptionally be due to the presence of some coccus or bacillus, *e. g.* pneumococcus, or of Vincent's organisms (*Pseudo-Diphtheritic Tonsillitis*). The first two and the fourth of these varieties of tonsillitis are not specific, but are probably always associated with microbic infection, often of a multiple character, and are usually more or less contagious. Tonsillitis forms one of the multiple lesions of scarlatina and of measles. It is also antecedent to every quinsy.

The tendency in former times was to concentrate effort on the local rather than on the general constitutional treatment. To-day strong antiseptic pigments are considered worse than useless because not only do they not reach the septic crypts, but they increase the pain. This is generally correct, but in the very early stage of cases of recurrent tonsillitis it is sometimes useful to apply pure guaiacol, after previous cocainisation, to the surface of each tonsil to try and abort the attack, a not unusual sequence when the lesion is still superficial. Gargling is painful and probably useless, even if the patient makes a conscientious effort to carry it out. Warm mouth-washes of listerine or glycothymoline tend to cleanse the mouth and the teeth and are always soothing. Atomised cocaine is disappointing in small doses, and may affect the heart and cause insomnia in large ones, and it causes a feeling of increased tumefaction. Alkaline sprays are useful when there is much ropy mucus clogging the fauces; nothing is better than nebula alkalina applied by means of a De Vilbiss coarse atomiser with an adjustable nozzle. An atomised solution of permanganate of potash is useful when there is much fœtor and sepsis. Demulcent and anodyne pastilles sometimes do good; antiseptic lozenges are probably useless, and when they do appear to relieve—as, for instance, the carbolic acid lozenge—the effect is due to the analgesic rather than to the antiseptic action of the drug. Chloretone, orthoform and morphia insufflations are not so useful in very painful cases of tonsillitis as they are in throat conditions where the surface is broken and ulcerated. External hot applications are always comforting, however applied; Leiter's continuous cold coil was once almost a routine measure in the practice of some throat specialists, but hot water is now substituted for the cold. Relief of pain during the taking of fluids is sometimes afforded by some one standing behind the patient and making firm pressure with the hands on the ears and side of the jaws during the act of deglutition.

Although the general treatment is so much more satisfactory than any local symptomatic treatment, yet it can be summed up in a few words, viz. an initial purge of calomel followed by a saline, the frequent administration of aspirin or allied drugs, and a cautious resort to a hypodermic injection of morphia and atropine to procure sleep and relief from excessive pain. Therapeutic inoculation should be resorted to where the disease is due to a specific organism, *e. g.* antitoxin in diphtheria, or a stock serum, followed by an autogenous vaccine in severe or recurrent cases where micro-organisms such as the streptococcus, the micro-coccus catarrhalis, the pneumococcus, Friedlander's bacillus, or the influenza organism are found to predominate. Where Vincent's organisms are present the result of vaccine therapy has been rather disappointing in my hands; the application of powdered salvarsan is now employed to kill the spirochœtes. If the exudation is long continued the disease is best got rid of by complete excision when the inflammation becomes subacute. If cases hang fire during the *subacute stage*, especially if there have been previous attacks, the question of complete excision should arise, and in recurrent cases this is clearly indicated during the quiescent period. The rheumatic factor in some cases must be borne in mind.

During convalescence, especially in anæmic subjects, iron preparations may be needed. Each convalescent, however, will require treatment according to the special indications of the case; but as relapses are not uncommon, and as the state of debility often leads to the recurrence of other dormant troubles, it is well to bear in mind that to continue treatment during the stage of recovery, and after, is not the least important function of the practitioner in dealing with a case of severe tonsillitis.

Quinsy (Palatine or Peritonsillar Abscess) is the popular name for an acute tonsillitis *plus* a peritonsillar or epitonsillar (palatal) abscess. An acute true intra-tonsillar abscess is extremely rare, the writer having only met with two unequivocal cases; the reason is to be found in the structure of the gland, which is riddled with crypts or lacunæ, whereby the discharge of inflammatory products out of the mouths of the lacunæ is facilitated. In cases of acute tonsillitis, however, an extra-tonsillar abscess often forms in the palate above the superior pole of the tonsil, and sometimes externally and posteriorly between the planes of the pharyngeal portion of the deep cervical fascia. Acute tonsillitis with a super-added adjacent peritonsillar abscess constitutes a quinsy. Infection is supposed to penetrate the capsule into the epitonsillar (palatal) cellular tissues from the *crypta magna* or "tonsillar recess," which opens into the supratonsillar fossa. Some authors consider that an abscess may occasionally form in the "recess" itself by

the blocking of its mouth by parenchymatous swelling accompanying acute tonsillitis.

The patient is unable to drink, eat, expectorate or cough without pain, and, as sleepless nights are super-added, complete mental and physical prostration soon results in severe cases. These symptoms rapidly disappear in most cases after evacuating the pus by an incision through the anterior pillar or through the most prominent part of the bulging palate. Incising the tonsil itself is useless, and endeavouring to evacuate the abscess by means of an angular metal searcher or director inserted into the tonsillar recess is extremely painful and unsatisfactory from the point of view of hitting off the abscess cavity, and of subsequent drainage. Tonsillectomy has been recommended, but not often practised. The pus having been found by a palatal incision, sinus forceps are inserted and opened and the abscess evacuated by pressure; this can be followed by injection of hydrogen peroxide. Should prompt incision be refused, heat externally and mouth-washes may possibly hasten the bursting of the abscess, as subsidence rarely happens; spontaneous evacuation takes place either between the glosso-palatine fold and the superior pole of the tonsil, through or in the region of the tonsillar recess, or through the palate, and very exceptionally behind the pharyngo-palatine fold. When the last happens, the case has probably been complicated by a lateral pharyngeal abscess; the latter condition may, in fact, have been the prominent feature throughout. There is said to be a danger from septic pneumonia when abscesses burst during sleep from inhalation of pus. After the evacuation of the palatine abscess the symptoms may only be partially relieved, and there may be an apparent relapse. In these circumstances search should be made for a *lateral pharyngeal abscess* behind the pharyngo-palatine fold; this complication is rare, but, if found, should be opened from the pharynx by means of a pair of angular scissors or an angular bistoury; an external cervical operation is rarely necessary. Exceptionally a second abscess may form above the opposite tonsil at an interval of some days from the appearance of the first. General *septic phlegmonous or œdematous inflammation of the pharynx*, often extending to the larynx, a highly dangerous condition, may be mistaken for a quinsy; it is rarely, if ever, a complication of a true quinsy, and is more probably always a distinct disease *ab initio*, being characterised by a tendency to spreading œdema, rather than to the formation of a localised abscess. A quinsy is, of course, in the first instance a localised phlegmon, and it is a moot question whether incision is advisable before there is evident pus formation. Although most authorities advocate incision when there is evidence of abscess, it is fair to state that Harmer is opposed to surgical interference, and holds that patients suffer less if the abscess is allowed to take its course and either burst or subside.

After complete recovery the question of excision of the tonsils should be considered in cases of a recurrent quinsy, as the cause of this is usually to be found in a septic condition of the crypts (chronic lacunar tonsillitis). As the glands in the neck are frequently inflamed in quinsy, the danger of chronic cervical adenitis as a sequela should be urged when the patient is inclined to refuse early palatine incision.

Enlarged Tonsils—Simple Enlargement of the Tonsils without Lacunar Deposits—Chronic Inflammatory Enlargement of the Tonsils.—Children with considerably enlarged tonsils often enjoy good health, and if the tonsils are only moderately enlarged, give rise to no symptoms and are free from septic matter in the crypts, there seems no urgent reason for surgical interference; should, however, deafness, mouth breathing and other symptoms be present, and should there be enlarged glands in the neck or a history of recurrent attacks of acute tonsillitis, or of peritonsillar abscess (quinsy), then excision and the completer the better, is indicated, together with the removal of adenoids, if present. Whillis' guillotine method is now largely adopted in this country and America. This can be carried out by any rigid guillotine, but there is an advantage in using Elphick's modification of Ballinger's instrument, as it has two blades, one for crushing and enucleating the tonsil entire in its capsule, and another sharp one for severing it from the crushed stump.

The important question of latent tubercle bacilli in the crypts of enlarged tonsils has brought forth most contradictory opinions. Whereas Levy and Chiari found that in 1085 patients actually suffering from laryngeal tuberculosis there was clinical evidence of tuberculosis in less than two per cent.; on the other hand, Wood gives 69 per cent. of tuberculosis cases examined as suffering from tonsillar tuberculosis. The discrepancy is probably to be explained by the want of distinction between clinical and latent tuberculosis of the tonsils. Still, considering that the tonsils are amongst the acknowledged avenues of entry of tubercle bacilli into the system, Wood's statistics are sufficiently disquieting, and many for this reason prefer to advise removal of enlarged tonsils unless there are special *contra-indications*, *e. g.* in hæmophilic subjects, and in cases of anæmia, status lymphaticus, leukæmia, cardiac disease, epilepsy, or extreme debility where an operation might be dangerous from shock, or other reasons.

In the latter circumstances especially, various

alternative measures to operation have been advocated from time to time; they are none of them to be depended on in large and hard tonsils of long standing, but are sometimes of some use in soft enlargements, more especially in recent cases following an acute attack of tonsillitis. Climatic treatment includes residence at places like Margate and Broadstairs, or a sea voyage. Preparations of iron, arsenic, iodine and phosphorus, singly or in combination, are largely used in recent cases; the iodide of iron, and such preparations as Parrish's Food, the syrup of the hypophosphites, malt extract, and cod-liver oil, appear to effect a real reduction in some instances in children. A measure of success has been claimed for lymphatic gland extract.

The employment of pigments containing either iodine, tannin, iron, creasote, carbolic acid and silver, while not such a routine measure as formerly, is still frequently carried out; personally I have abandoned the use of paints in simple enlargement of the tonsils, that is without septic crypts, and I regard any improvement observed under this treatment as rather in spite of the painting than because of it.

The employment of X-rays has recently been advocated by Steuart, for the reduction of soft, enlarged tonsils remaining over from an acute inflammation, and in cases where operation is contra-indicated. It is also claimed that the accompanying hyperplasia of Luschka's tonsil (adenoid growths) also undergoes a substantial reduction in many cases. Whether the method is likely to prove to be worth, even as a palliative measure, the trouble and the expense involved in several sittings it is as yet too soon to say. The technique is described under the heading of special therapeutics of the fauces and pharynx. Radium treatment might be expected to do all that is claimed for the X-rays, but the method by long exposures with a special apparatus would be impracticable in children quite apart from the question of expense and availability.

Chronic Lacunar Tonsillitis.—In this condition there are septic deposits in the lacunæ which keep up pharyngitis with one or more of the following, viz. sore throat, aching throat, a recurrent pricking sensation in the fauces, the feeling of a foreign body being present and both objective and subjective fœtor.

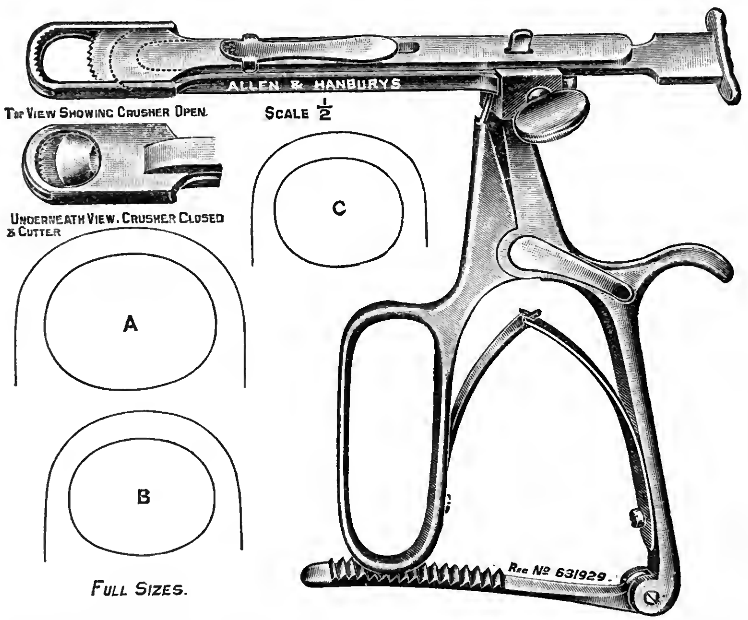


Fig. 9.—Elphick's enucleating guillotine with two blades, one for first enucleating the tonsil from its bed, crushing the stump, and the other a sharp one for severing the tonsil.

A genuine chronic lacunar abscess forms in some instances recurring at regular or irregular intervals and ending by the extrusion of a foul caseous core. The tonsils may or may not be markedly enlarged. The local and general treatment, without resorting to surgical interference, includes that already detailed under the heading of simple enlargements of the tonsils; but more attention is usually paid to local applications such as painting with either guaiacol, resorcin, glycerine of carbolic acid, iodine or menthol. It is, however, doubtful if these remedies ever reach much beyond the mouths of the crypts and they cannot penetrate to the depths of these recesses—when the disease is of long standing and general constitutional treatment together with change of air has been given a fair trial, there is only one satisfactory method of treatment and that is *complete* surgical removal of the tonsils, a dissection being necessary when the tonsils are buried in adherent pillars. Operation should never be delayed when the cervical glands are enlarged. If a cutting operation is contra-indicated galvano-cautery puncture carried out at several sittings may be tried. Dealing with isolated crypts in this manner or by slitting up is not recommended when there is no real objection to complete excision either by the guillotine or snare or dissection. As has been before stated, it is the septic state of the crypts rather than the size of the tonsils

which should be the guide in recommending complete removal.

Tonsillar Hæmorrhage. — Considerable bleeding immediately following tonsillectomy with short anæsthesia, which does not cease spontaneously after a few deep breaths, usually does so after syringing with ice-cold water; if this fails hot water syringing should be tried. General parenchymatous bleeding is best dealt with in the first instance by pressure, a pad of cotton-wool or lint dipped in hydrogen peroxide or adrenalin solution or in a paste of equal parts of tannic and gallic acid being pressed with the end of a pair of long forceps against the bleeding area for ten or even twenty minutes. Watson Williams' special forceps with one blade against the tonsil and the other outside near the angle of the jaw, is especially handy for this purpose. Pressure with the finger instead of the forceps is tiring but very efficacious. Applications of iron should be avoided, as they usually fail and a dirty sloughing surface results. Styptic collodion was at one time much recommended, but it is painful and rarely efficient, and gives rise to a

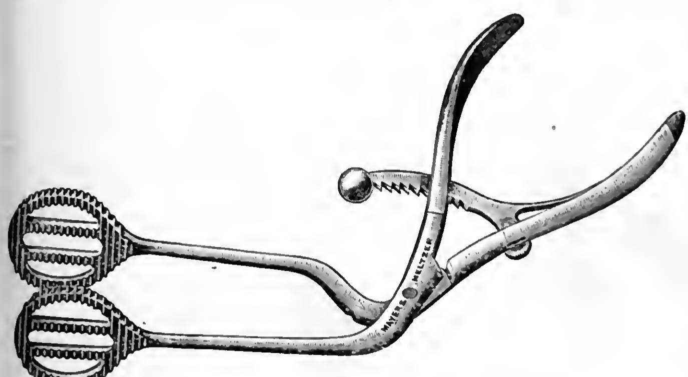


Fig. 12.—Watson Williams' Tonsil Forceps.

great deal of irritation and cough if any of it touches the epiglottis.

A spurting vessel can be clamped with a long pair of artery forceps and ligatured later if necessary. A special forceps with broad vertical blades for temporarily clamping the two pillars together is so useful and efficacious that it ought always to be at hand. If on removal of this forceps after half an hour bleeding begins again, it will save further loss of time to sew up the two pillars over a roll of lint dipped in styptic. This can be accomplished either by a long curved needle, or by a cleft palate needle, or more easily still by using Michel's hooks.

The instrument for closing the hooks and removing them the next day are here illustrated. If each hook has a silk ligature attached to it,

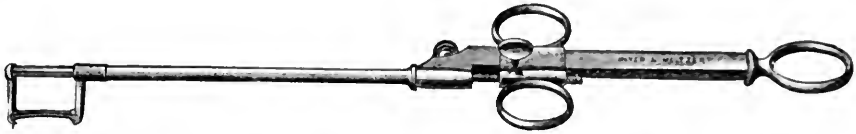


Fig. 10.—Instrument for suturing pillars of fauces with Michel's hooks.

Fig. 11.—Forceps for opening and removing Michel's hooks.

and the end secured outside the mouth, there will be no danger of trouble if the hook eats through. The drawback to applying Michel's hooks is that septic œdema of the fauces and palate is apt to supervene, and the same may follow the prolonged application of forceps and, in a lesser degree, sewing up with the needle; these three measures, therefore, should only be resorted to when simpler means fail, and they should be discontinued as early as possible.

The writer has on two occasions brought about the immediate cessation of serious and long-continued bilateral tonsillar hæmorrhage by pressure on the carotid arteries with the patient lying on his back on the floor. As fainting occurred on each occasion the pressure may possibly have been exerted on the vagi as well, and it is impossible to escape the reflection that such pressure might not be altogether free from danger.

The placing of a temporary, or of a permanent, ligature on one external carotid has been resorted to on a few occasions, but can rarely be called for if instruments for dealing with the bleeding area are at hand.

The value or otherwise of calcium lactate, whether before operation or after bleeding has supervened, is a matter on which there is much difference of opinion. The internal administration of drugs for which a hæmostatic action is claimed, such as gallic, sclerotic and sulphuric acids, iron, tannin, ergot, ergotin,

opium, stypticin, is a method too slow and unreliable in action to be worth considering except in moderate prolonged oozing. In the latter circumstance there is no harm in injecting either morphia or ergotin hypodermically. Inhaling amyl nitrite occasionally seems to do good and can be used in addition to local measures. Subcutaneous or rectal saline injections, or even transfusion, may be necessary where much blood has already been lost.

Malignant Diseases of the Tonsils and Fauces.—The local treatment varies at different stages of malignant growths, but is more or less identical whether the disease be carcinoma, sarcoma or lymphadenoma. In early stages when limited to the tonsil, *i. e.* when it has not permeated the capsule, excision has been successfully performed from the mouth with or without slitting the cheek. When, however, the glands at the angle of the jaw are enlarged and the folds slightly attacked, nothing short of Vohsen's operation is likely to succeed. An incision is made from the mastoid tip to the hyoid and then carried upwards over the angle of the jaw; the lingual, facial and ascending pharyngeal arteries are ligatured, and the jaw divided in front of the masseter and the ascending ramus pulled strongly forwards out of the way; this gives good access to the tonsillar bed; enlarged glands may have to be dealt with by additional incisions. When the disease demands a much more extensive operation than this, the chances of successful radical removal are immensely reduced. When the growth nearly closes up the fauces so as to interfere with swallowing, articulation and respiration, partial removal with the knife, galvano-cautery or surgical diathermy is justifiable and may give much temporary relief. Serious recurrent hæmorrhage may follow the placing of a temporary or of a permanent ligature on the carotid. Those requiring first-hand information should refer to the articles in *Burghard's System of Operative Surgery* by Waring and Trotter.

Non-operative palliative measures include the use of the X-rays and the employment of screened radium salts, either applied to the surface for a period which will not cause ulceration, or embedded in the tonsil so as to attempt to bring about aseptic necrosis. The glands should also be treated. Radium is a most uncertain remedy, but apparent temporary disappearance of the growth has now been recorded in a number of cases, and in other instances there is marked reduction in the size of the growth and in the symptoms. Sarcomas, more especially endothelial sarcomas, appear to respond better than epitheliomas. Electrolysis is said to have been beneficial in a few cases of sarcoma of only moderate malignancy. When there is great narrowing of the fauces on account of the large size of the growth, much palliative success has been attained in producing aseptic necrosis of the bulk of the growth by the new method of diathermy, which produces a wound which heals well. This is in marked contrast to radium when used to the extent of cauterisation, after which there is often no tendency to healing and there may be increased pain. Injections of Coley's fluid and of colloidal preparations of copper and of selenium have done substantial good in a few cases only. The other palliative measures, local and general anodyne, are identical with those employed in superficial cancers in other parts of the body. (See also section on *Special Therapeutics of Fauces and Pharynx.*)

Malignant Disease of the Deep or Post-cricoidal Pharynx.—Cancer in this region, if diagnosed in the early stages, can be dealt with by excision of a part of the pharynx by lateral pharyngotomy if the growth is limited to the posterior wall. When the back of the cricoid plate or the pyriform fossæ are invaded the larynx must be removed as well. The treatment of inoperable cases by radium has already been discussed. The same palliative measures as those described under the heading of Cancer of the Tonsils and Fauces apply here.

Acute Septic Pharyngitis.—The milder forms of this condition have already been alluded to as occurring in conjunction with acute tonsillitis; these include: (1) the superficial catarrhal form, and (2) the ulcerative and membranous forms due to a streptococci, staphylococci, pneumococci, Friedlander's bacilli, micrococci and Vincent's organisms. The lesions may much resemble those found in true diphtheria and in scarlatinal diphtheria. Three more varieties which are especially malignant are occasionally met with, viz. (3) the spreading œdematous form with cellulitis which tends to spread to the larynx and tissues of the neck, but not leading to suppuration, (4) the phlegmonous or suppurating form of cellulitis, and (5) the gangrenous form. The last three grave forms are often grouped together on the ground that any of the various infective organisms above-mentioned either separately, or in conjunction, may give rise to any one or in succession to all three of these pathological lesions, viz. cellulitis, suppuration and gangrene according to the virulence of the infecting agent or agents. The general treatment differs little from that of acute blood-poisoning elsewhere, and the same possible complications have to be combated as regards pneumonia, pericarditis, endocarditis, nephritis, etc. The high fever, if present, must be reduced by appropriate remedies; the poisoned

circulation must be dealt with in the first instance by the administration of an anti-streptococcal serum or of a polyvalent serum to be followed by an autogenous vaccine; and the strength must be maintained by a supporting diet of beef tea, raw eggs and milk together with stimulants. An initial dose of calomel and the administration of a mixture containing iron and quinine is the recognised routine as regards drug treatment. Oxygen should always be at hand for inhalation.

The local treatment necessarily varies with the course of the case. Extension to the larynx may demand incision of the œdematous tissues of the vestibule, and this is probably to be preferred to tracheotomy—in itself an exhausting complication: multiple incisions, after applying cocaine and adrenalin to the œdematous laryngeal tissues, has given instant relief in several cases under my care, and since adopting this method I have not had recourse to tracheotomy, but it may be necessary when the œdema spreads to the trachea. The same procedure is sometimes called for in the fauces and pharynx. The formation of abscesses should be watched and dealt with either by external or internal incision. In addition to these necessary local measures some practitioners worry the patient by local applications, but they probably do more harm than good. A sedative spray or inhalation may be soothing and hot fomentations externally are worth trying. If there is great difficulty and pain in swallowing from the infective process spreading to the gullet it is sometimes easier than might be anticipated to pass a soft rubber tube into the upper part of the œsophagus and administer fluid nourishment through it. Other complications must be dealt with as they arise. Death may occur from the virulence of the toxæmia with cardiac failure, or from pneumonia, or from cerebral symptoms, or impaired renal action. Bearing in mind the gravity of the toxæmic factor which overshadows the mere local lesion, the importance of early and skilled treatment by therapeutic inoculation measures cannot be too strongly insisted upon in all cases of pharyngitis of obscure etiology with spreading œdema, fever and albumen in the urine.

Chronic Pharyngitis.—It is usual to divide up chronic inflammation of the mesopharynx into two groups, the hypertrophic and the atrophic. The former, again, is subdivided into: (1) the simple catarrhal form with moderate thickening of the mucosa and hyper secretion; (2) the marked hypertrophic form with general thickening of the mucosa, submucosa and even muscular coats, more especially of the soft palate, folds of the fauces and salpingo-pharyngeal folds; (3) granular pharyngitis in which the thickening is limited to the islands of enlarged lymph tissue on the posterior wall and (4) lateral hypertrophic pharyngitis in which the salpingo-pharyngeal fold and the pharyngo-palatine folds are the regions enlarged. All these forms of hypertrophic pharyngitis are frequently associated with nasal obstruction and mouth breathing, and the relief of the former is often not only a necessary part of the treatment, but all that is necessary in the way of treatment. In many cases, however, there is either no marked nasal obstruction or the pharyngitis remains when the nasal lesion or lesions have been appropriately treated. The treatment must depend to a considerable extent on the exciting cause, and in few conditions is it so difficult as in a case of chronic pharyngitis to ascertain this with certainty, as the possible etiological factors are so many and varied and often remote. Local septic conditions of the teeth, mouth and tonsils may require attention. An elongated uvula, though a result of chronic inflammation, may become a factor in keeping it up by inducing cough and hawking. Pharyngitis is both caused and kept up by excessive discharges from the lower air-passages in the same way as it is from the upper air-passages. The pharyngeal mucosa is often sympathetically affected in various gastric disorders and in alimentary toxæmia; it is also frequently congested in cases of cirrhosis of the liver and in renal disease. Amongst more widespread morbid conditions must be mentioned gout, chronic rheumatic states, anæmia and sclerosis. Amongst extrinsic causes must be mentioned frequent exposure to inclement or irritating atmospheric conditions including the inhalation of irritating particles in connection with occupations. Tobacco-smoking and excess of ardent spirits no doubt in some measure account for chronic pharyngitis being much more common in men than women, more especially in hospital patients.

Treatment directed towards any one or several in combination of the above-mentioned causes may in fortunate circumstances lead to a cure without resort to local treatment. The latter is, it must be confessed, little more than palliative in many of the very chronic hypertrophic conditions, and no topical treatment can be expected to reduce a long-continued thickening of tissues which has extended even to the muscles, and chronic congestion is often equally intractable. When the latter is associated with constipation and portal congestion, considerable relief is often afforded by an alkaline coarse spray or douche, either hot or cold, in conjunction with the morning administrations of Carlsbad salts and purgative waters. These are the cases which are often successfully

dealt with at various spas such as Ems and also at Harrogate where the local treatment of the pharynx is carried out by the Ems method. In granular pharyngitis the reduction of the prominent islands of lymph tissue is generally regarded as a necessary routine treatment, but except where there is accompanying hyperæsthesia or paræsthesia which burning may blunt, it is doubtful if the cautery does much good. Iodine in the form of Mandl's solution is highly thought of by many practitioners, but I have usually found it disappointing. The same may be said of the local application with the brush of caustic solutions of nitrate of silver, protargol, argyrol, zinc chloride and copper sulphate. Astringents are certainly useful in sprays or douches in temporary relaxed conditions with excessive secretion. One or more of the various local anodyne and sedative remedies discussed in the sections dealing with sprays, douches, gargles and lozenges should be tried when there is pain, aching, soreness, irritation or cough. The latter in conjunction with hawking are especially liable to increase congestion. Finally it is important to rectify as far as possible any errors of diet and general hygiene; and faulty methods of vocal production, more especially in the case of professional voice-users, may require rectification at the hands of an expert in such matters.

Atrophic Pharyngitis in its advanced form is even more resistant to curative treatment than the markedly hypertrophic form, as the atrophied mucosa, together with its glands and blood-vessels, cannot be regenerated. Local palliative treatment together with general constitutional and hygienic measures give relief in some cases.

The disease is frequently an extension of the same pathological condition in the nose or else is associated with suppurative discharges from the nasal sinuses. Intranasal inspection and treatment, therefore, is of prime importance. Local measures in the pharynx are mainly palliative, and consist of removing, at least once or twice, and often many times, daily the sticky muco-purulent discharge and crusts which adhere to the mucosa of the posterior wall of the naso-pharynx. This is best effected with a brush charged with a paint containing either boro-glyceride, or menthol, or paroleine or glycerine. A creasote vapour beforehand is said to aid in the detachment by the brush. An alkaline coarse spray or douche, or menthol and thymol dissolved in paroleine applied through a special atomiser serves to finish up the toilette, and also to lubricate the mucosa and prevent readherence for some hours. Stimulation of the semi-atrophied glands by iodine paint locally and by iodide of potassium given internally undoubtedly relieves for a time in some cases, but this treatment should not be long continued as it may tend to increase the atrophic process. Menthol for the same reason should not be applied too strong and should be employed carefully and intermittently. Anæmia, dyspepsia, intestinal stasis and other departures from health, must be as far as possible rectified. Arsenic and arsenical waters are said to be occasionally of marked value, but must be administered with caution, well diluted and on a full stomach. There is considerable difference of opinion as to whether treatment at the sulphur spas really modifies or arrests the condition. It has been claimed that the bromo-iodine impregnated mud of Weston-super-Mare has a beneficial effect on young people suffering from atrophic rhinitis and pharyngitis who go to reside there.

SPECIAL THERAPEUTICS OF THE ŒSOPHAGUS

The treatment of morbid conditions of the gullet is mainly surgical rather than medical and of the nature of endo-œsophageal manipulative and surgical measures carried out with the *aid of the œsophagoscope*. General constitutional treatment is of limited usefulness, and often little more than expectant even in the more purely medical diseases such as those associated with nerve lesions and with the rare forms of œsophagitis due to the extension of septic œdema from the throat, to thrush, to diphtheria, to scarlet fever and to tuberculosis. On the other hand, in syphilis, which very exceptionally affects the gullet, the treatment is mainly medical in the first instance in active lesions and should be successful.

The following measures though largely manipulative may be considered as coming within the scope of this work—

1. The local application of sedatives and analgesics, and of lubricants, etc.
2. Endoscopic bougieing and the use of dilators.
3. The employment of feeding-tubes and of intubation.
4. Electrical methods.
5. The application of radium.

The Œsophagoscope as an Aid to Treatment.—The importance of the endoscope for the accurate diagnosis of lesions in the gullet is now becoming generally recognised, but it is almost as indispensable in treatment. Only by its aid should foreign bodies be removed, strictures be dilated and local applications made to ulcers, and radium tubes applied to cancers if accuracy, celerity and safety are to be combined. In many tolerant cases œsophagoscopic procedures

can be carried out by an expert under cocaine anæsthesia, aided by morphia and atropine; but in a considerable number of instances a general anæsthetic is either advisable or absolutely necessary where difficult or possibly dangerous manipulations have to be performed.

Local Sedative Applications. — Unlike the pharynx, local applications cannot be made either by unaided direct visual inspection or by the ordinary throat mirror as the gullet commences at the level of the lower border of the cricoid cartilage. For the mere application of sedatives and analgesics the use of the œsophagoscope is neither desirable nor necessary. Sprays of cocaine and powders of chloretone, orthoform and morphia insufflated into the back of the pharynx will be carried by the intermittently swallowed saliva down to the painful areas in the gullet and there exercise a local action. Another method, and one which insures a more lasting effect on the inflamed and ulcerating areas is to mix up one or other of the powders mentioned into a paste with bismuth oxychloride which tends to stick to the strictured regions, *e. g.* in carcinoma, for a considerable time, thereby effecting a more prolonged local action. I have noticed that patients suffering from ulcerating cancers or from ulcers resulting from the impaction of foreign bodies or from injuries, and from other forms of acute œsophagitis, have been relieved by the swallowing of bismuth paste which has been given in connection with a radiographic examination. Bismuth emulsion or bismuth made into a paste with a little water is therefore the ideal medium or base for the administration of analgesic powders.

Patients with stricture, especially the cancerous form, experience great discomfort and impaired swallowing power from the presence of a large quantity of frothy mucus and saliva in the dilatation above the stricture; relief can sometimes be obtained by administering the compound spirits of ether (Hoffman's anodyne) from 1 or 2 dr. being diluted with as little water as the patient will tolerate. This reduces the froth by diminishing surface tension, and it also has a local anæsthetic and antispasmodic action.

Lubrication of the gullet by means of liquid vaseline, refined petroleum and other oily fluids is sometimes useful in dysphagia by helping the bolus of food to slip through the strictured region. Anodynes can be advantageously added just before a meal.

Lavage daily with a solution of soda is very useful in large dilations above a stricture in cases where a pint or more of fluid, *e. g.* tea, is largely retained for an hour or so after swallowing on account of its only slowly trickling through into the stomach. Washing out the gullet above the stricture gets rid of solid food long retained which adds to the obstruction. In one case of cancer I removed a portion of mutton which had been retained since the last occasion that meat had been taken three weeks before. Lavage with Condy's fluid is also beneficial and sedative in ulcerative conditions and serves to diminish the characteristic fœtor in cancer. In cases where the stricture is not sufficiently tight to hold up fluids, I have devised a plan for efficient lavage which consists in sealing up the distal orifice of the red rubber tube and making another hole three or four inches further up; the terminal part of the tube is then passed into and tightly engaged by the upper part of the stricture, and fluid can be passed into the dilatation above and aspirated out again. Solutions containing peroxide of hydrogen should not be employed, as the frothing which takes place in the presence of blood, pus and débris may cause unpleasant respiratory obstruction by overflowing into the air-passages. Lavage is, of course, contra-indicated in perforations into the trachea or bronchi.

The Employment of Bougies. — The blind passage of bougies for the purpose of either diagnosis or treatment is now generally condemned by œsophageal experts, though the method is still largely resorted to by general physicians and surgeons and by family practitioners who fail to recognise that as a diagnostic agent it is inferior to the X-rays and rarely of any differential value, and is not free from an element of danger. It is true that fatal results and minor injuries are only exceptional occurrences, and it must be admitted that blind bougieing frequently affords great relief in many cases of stricture, but the risks are much greater than when the method is carried out aided by vision, through the œsophagoscope and the results are far better by the latter method, as it is possible to dilate up quite a tight stricture after localising its upper orifice by direct vision through the endoscope.

After, in the first instance, localising and dilating up a non-malignant stricture with the aid of the œsophagoscope it may be permissible in some cases subsequently to employ the bougie blindly; but this must be done with much circumspection even by experts. After per-endoscopic dilating by means of graduated bougieing not only is dysphagia relieved temporarily, but a stricture can be rendered sufficiently patent to allow of other methods of treatment such as temporary or permanent intubation or the application of radium; the latter is specially indicated in cancerous lesions of moderate extent. In very tight strictures a small gum elastic bougie two or three millimetres in diameter is gently insinuated through the stricture after the upper end of the latter

has been localised by direct vision through the œsophagoscope. Shifting the curve of the dorsal spine so as to straighten out the gullet will often aid this. When a small bougie has been successfully passed it is usually possible to dilate up the stricture so as to admit of one of eight, nine, or ten millimetres in diameter, when once the correct line has been got, by passing larger and larger bougies allowing each to remain a few minutes *in situ* if gripped. If great difficulty is experienced in getting at first a small bougie through, another small one should be passed alongside the other and allowed to remain a few minutes before withdrawing the first one and passing larger ones.

In America a strong thread with a shot at the end is much used as a guide. Several yards of thread are slowly swallowed, and when it has passed well into the intestines so as to become moored it serves as a guide when made taut for the passage of hollow bougies and dilating bags. I have found it useful to attach a dozen large shot to the thread so as to ascertain by the X-rays when they have passed sufficiently far into the ileum to allow of traction being made.

The patient in some instances should, if possible, be taught to pass soft rubber stomach tubes of suitable size himself two or three times daily after a tight stricture has been dilated up by endoscope bougieing with gum elastic sounds. These red rubber bougies can do no harm, but on the contrary may do much good if the patient can manage to pass them. When an organic stricture in the phreno-cardiac portion of the gullet has been dilated up by graduated bougieing or by a dilating apparatus, there is difficulty in the ordinary rubber feeding-tubes finding the upper orifice of the strictured lumen as the gullet above the stricture is often greatly dilated; in such circumstances I have employed with success a rubber feeding-tube with the orifice at the lower end sealed up and the tube filled with metallic mercury; if the patient makes the act of swallowing when the lower end approaches the strictured area the weight of the mercury will often greatly assist the passage of the tube into the stomach. If the patient can tolerate it the tube should be left *in situ* for half an hour, so as to exercise a further dilating effect.

Dilatation by Expanding Instruments.—The method of dilating up organic strictures by the passage of larger and larger bougies through the œsophagoscope at one sitting, has already been described. The advantages of continuous dilatation by the wearing of an intubation apparatus subsequent to bougieing will be dealt with more fully in a later section. Immediate dilatation by forcible methods are not largely resorted to. Brunings and Abrand employ expanding metal dilators, on the same mechanical principle as those used in the rectum and urinary passages in cicatricial strictures, more especially at the lower end of the gullet. They require to be used with great caution. I have myself resorted to this method on a few occasions, and in one case of fibrous stricture of the phreno-cardiac region of the gullet I caused a rupture below the diaphragm. The patient experienced great pain on swallowing a test draught of sterilised water a few hours after the dilatation, which was performed under an anæsthetic. He was therefore kept on nutrient enemata for three days and again tested when water caused no pain and food was resumed by the mouth. There were early symptoms of a localised abscess below the diaphragm; this, however, was not opened by laparotomy till it showed signs of having advanced nearly to the abdominal wall, as evidenced by œdema at the left costal margin near the sternum. The patient's dysphagia was, fortunately, very substantially relieved in spite of the mishap.

On the Continent Gottstein's pneumatic dilators are sometimes used; and in America Plummer and others claim great success in moderate tumefactive strictures near the cardia, the so-called cardiospasm, with rubber bags expanded by mercury forced in under pressure, but regulated by a manometer. Ruptures, however, have been occasionally recorded after these methods also, and all these forcible procedures are probably more dangerous than internal œsophagotomy. Dilatation by graduated bougieing carried out through the œsophagoscope under an anæsthetic followed by temporary intubation should be the method of choice in most cases.

Tubage and Intubation.—Both temporary and long-continued intubation are of great value in both acute and chronic strictures however caused. The simplest form of tubage consists in the passage of a soft red rubber feeding-tube through the narrowed region each time it is desired to feed the patient. This is particularly serviceable where there is painful swallowing in those exceptional cases such as acute œsophagitis due to microbic inflammation or to slight trauma after manipulations. It is also used after operations about the laryngeal orifice and deep pharynx, and in severe forms of dysphagia, due to tuberculosis or to paralysis.

The retention of a feeding-tube for a few days or for weeks or for more prolonged periods is employed not only to relieve dysphagia and even aphagia, but also for the "bougie effect" in bringing about increased patency for a time in chronic inflammatory and in escharotic and other cicatricial strictures, and also to maintain patency after the surgical treatment of stenosis in any form. It is also useful for

dilating up a cancerous stricture preparatory to the application of radium.

The retention of a small gum elastic catheter either temporarily or permanently was advocated by Krishaber at the International Medical Congress in London in 1881. This method was immediately afterwards adopted by Croft and by Durham with considerable success, and has been occasionally practised from time to time by others even up to the present day, as I can personally testify. Morell Mackenzie modified the method by using an entirely endo-œsophageal gum elastic tube, funnel-shaped at its upper end and of small calibre (6 mm. in diameter) which was held in position in the strictured part of the gullet by suspending strings attached to the teeth; this was the forerunner of the very valuable intra-œsophageal method of Charters Symonds whose well-known gum elastic funnel, much larger than Mackenzie's, is mainly retained in position by reason of its shape which prevents its being swallowed in many instances; strings should be attached to the teeth or elsewhere outside the mouth in cancer cases, to prevent its slipping down and becoming buried in the stricture and also to enable it to be withdrawn. Strings can now be dispensed with in tight non-malignant strictures as endoscopy enables one to select a funnel of such a suitable shape and size as will not slip down through the stricture, and with the œsophagoscope the funnel can easily be removed when it is desirable to insert a fresh one for purposes of cleanliness, or to substitute a longer or a larger funnel. The white-coated gum elastic materials used in France are an improvement on the usual English make, as they tend to retain their shape longer and do not become sodden so soon. Jackson and Guisez use rubber œsophageal funnels, and there might be an advantage in substituting celluloid or vulcanite for gum elastic material because less liable to decomposition; there might be, however, a disadvantage in their rigidity compared with the more pliable rubber and gum elastic tubes. Symonds' funnel has been of great service in many hands and in many cases, and modern endoscopic procedures, so far from tending to displace altogether this form of intubation in median thoracic strictures, have in reality widened the field of its applicability by enabling us to dilate strictures more efficiently to a size capable of admitting the lower tubular part of the funnel, and a whalebone or other guide (minus the handle) can be first inserted more easily through the œsophagoscope, thus facilitating introduction. Symonds' funnel, however, cannot at first at all events be employed in very tight strictures which are incapable of much immediate dilatation by endoscopic bougieing, though after the reduction of the obstruction by radium, or by wearing the styletted tube it may later become possible to insert the funnel with advantage.

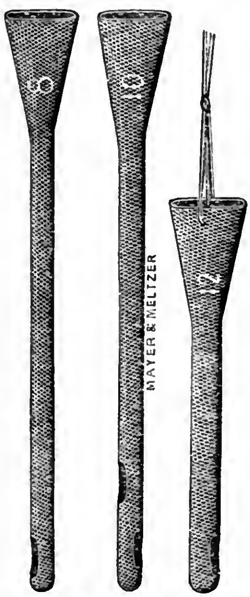


Fig. 13.—Symonds' gum elastic funnels for œsophageal stricture.

In stricture near the upper end of the gullet the funnel is not well borne, and in those near the phreno-cardiac region of the œsophagus the viscus is usually too dilated above to keep the funnel in position and prevent its being forced upwards out of the stricture. It is in these cases of tight strictures in whatever position, but especially in those near either end of the gullet, that an oro-œsophageal or an oro-gastric red rubber drainage tube of small calibre has proved such an efficient substitute for the funnel. Such a tube was, I believe, first employed in this country by James Berry over thirty years ago; the principle was a good one, but its introduction through the stricture was often very difficult even by the so-called railway method, and having no style, it was often either coughed or vomited up and then had to be re-introduced by a skilled hand. The tube was attached to the teeth or otherwise secured outside the mouth to prevent its being swallowed. This difficulty of introduction of a rubber tube was considerably reduced by Symonds when he brought out his modification of Berry's tube which somewhat resembles in shape a long Jacques urethral catheter, the passing of which is effected by means of a long thin whalebone guide lying along the *outside* of the catheter with the exception of the tip which is inserted into the eyelet; the guide can be removed

without disturbing the tube when the latter is *in situ*. Symonds' tube (which must not be confused with Symonds' funnel) has been used by me with success on several occasions; in some instances, however, it was either vomited or coughed up, the latter being especially prone to happen when there is a communication between the gullet and the air-passages: I was therefore led to devise a tube with a resilient style as a backbone, so to speak, to give it some measure of rigidity, and by which it could be attached to the teeth so that it could not easily be ejected by even the severest vomiting or coughing. At first I used a flat whalebone style passing through the whole length of a double tube. Such an apparatus was retained in a case of perforation for ten weeks. Later, I tried a soft silver flexible style instead of whalebone. The silver style tends to corrode and break in course of time, but its life is sufficiently long, varying from five to fifteen weeks. This styletted oro-œsophageal or oro-gastric intubation apparatus is generally easily introduced after endoscopic bougieing through the œsophagoscope, so that the question of putting in a fresh tube need not be considered on the grounds of difficulty. Patients can at first be fed with liquids only *through* the tube, but after a few days the "bougie effect" usually enables them to swallow fluids *by the side of the tube*, and later

Fig. 14.—Symonds' soft rubber œsophageal tube; a leaden plug, A, closes the proximal end, B; the hole placed laterally at the distal end is only faintly shown.

Fig. 15.—Showing whale-bone style, the end of which is inserted into the distal lateral hole of the Symonds' tube to facilitate introduction through the gullet stricture.

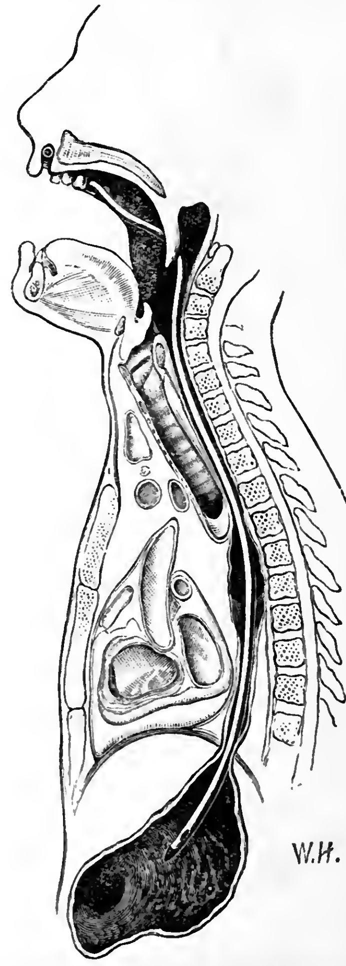


Fig. 16.—Hills' styletted oro-œsophageal feeding tube, which can be retained for a few days or permanently in œsophageal stricture; the proximal end can be secured to the teeth or to a denture.

soft food and even fat bacon, calf's head, tripe and onions and in some cases an ordinary meal can be got down quite easily in this manner. Although in advanced cases the tube has to be retained permanently, in others it can be left in for a week or two until owing to the bougie effect the patient swallows fairly well by its side, when it can be advantageously removed until the dysphagia again becomes troublesome. Of course patients are always very glad to get rid of the apparatus for a time, but it is generally well borne, and in only a few instances of cancer at the mouth of the œsophagus and deep pharynx do I remember serious pain and discomfort being complained of. The continuous bougie effect is of great importance because the patient frequently manages to swallow his saliva and thus is relieved from the constant expectoration of frothy mucus which sometimes amounts to many pints in one day and which is often such a distressing complication after gastrostomy. In cases of perforation the method of feeding entirely through an oro-œsophago-gastric intubation apparatus is specially indicated for permanent use in order to prevent liquid nourishment entering the air passages and causing violent fits of coughing; these cases always suffer from a good deal of coughing and expectoration due to swallowed frothy saliva, but the discomfort is only moderate compared to that brought on by fluids entering the air-passages. In mid-thoracic strictures with perforation a Symonds' funnel is in those cases where it can be inserted, to be preferred to a long oro-œsophageal or an oro-gastric tube, as the funnel shuts off the alimentary route from the air-passages.

Electrical Methods.—Treatment by electricity is little employed in the gullet. It is not of much service in the rare cases of paralysis of central origin. Functional neuroses are usually held to be of common occurrence, more especially in the form of œsophagismus and cardiospasm. The writer with a large œsophagoscopic experience has not found an unequivocal case of primary spasmodic stricture, though secondary spasm of the gullet evidenced by painful colic is often met with as a symptom of temporary tumefactive or of permanent organic stenosis when food is arrested. True functional dysphagia is usually due either to paresis or to a minor degree of subacute tumefactive œsophagitis. Paresis is best treated by bougieing, which has a stimulating action akin to the application of a brush or swab dipped in menthol paint in functional paresis of the pharynx and larynx. In peripheral neuritis, whether functional or otherwise, *faradism* would only be of possible service in the upper third of the gullet, where there are striped muscular fibres. In the lower two-thirds of the gullet, where the musculature is unstriped, faradism is useless and ordinary galvanism dangerous unless applied with special precautions to avoid an electrolytic action. The *sinusoidal current* is, however, free from danger, but any good result occasionally following its application may be partly due to bougie effect and partly to suggestion. It is probably useless in restoring tone to a dilated œsophagus which is regarded in some quarters as its chief indication.

Ionisation has been carried out very occasionally in organic strictures of the gullet, but the great difficulty in limiting its field of action seems almost to contra-indicate its employment. The same remark applies in a lesser degree to other destructive electrical methods, such as electrolysis, galvano-cautery and diathermy. The electrolytic method is, however, largely used by so experienced an œsophagoscopist as Guisez in fibrous strictures as an adjunct to forcible stretching.

The X-rays.—Whilst Roentgen radiography should be employed in most cases of suspected œsophageal disease for diagnostic purposes, it is little used therapeutically for the reason that the major part of the viscus is enclosed in a bony cage and is remote from the surface. In a few instances, however, it has been claimed that dysphagia due to carcinoma has been substantially relieved by this method of radiotherapy, more especially in lesions of the upper third of the gullet.

Radium Therapy.—The radio-active rays of radium salts and of radium emanation and of mesothorium have now been given a trial in a considerable number of cases of malignant disease of the gullet. The method was first tried by Exner in 1904 with short applications of lightly screened radium bromide. He and Einhorn claimed palliative results. It was not, however, until Guisez of Paris in 1908 commenced to employ radium frequently in gullet cancer in conjunction with Dominici that this therapeutic agent was given an adequate trial. As the result of the publication of some encouraging palliative results by Guisez in 1909, I was induced to give the method a trial in the summer of that year, and I reported my first series of twenty-one cases in February, 1911. (See *Trans. Med. Soc. Lond.*, Vol. XXXIV. pp. 211–222.)

I felt justified in claiming temporary disappearance of naked-eye evidence of growth in three cases and remarkable improvement both objective and subjective in seven cases. There was also apparently some substantial improvement in seven other cases which might or might not have been due in some of them to the "bougie effect" of the radium apparatus in relieving the stricture. One of these cases, in which the diagnosis was based on œsophagoscopic and

microscopical examination, is still living and in very fair health, eight applications of radium having been made at varying intervals during the last four and a half years. After the

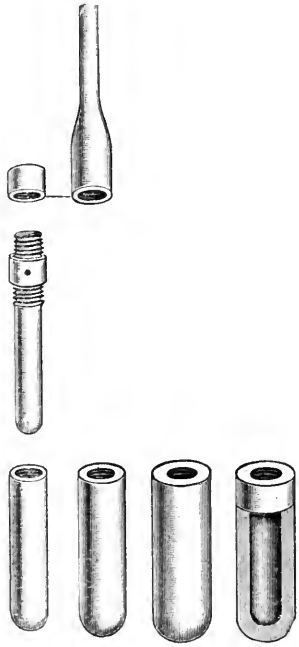


Fig. 17.—Finzi's Platinum tube containing 100 mgrms. of radium with style attached to the cap and additional metal screens, one of which has a window.

second application the fungating mass disappeared and the ulceration healed; there has been regrowth and ulceration observed on three occasions since. The swallowing has never been quite normal during the intervals when there was disappearance of objective signs as the lumen remained narrowed somewhat by fribrosis following radium. Another application had to be made quite recently.

The broad lines of technique employed by experts using radium in cancer of the gullet are the same. (1) The length of the stricture is ascertained by radiography after swallowing bismuth paste or thick bismuth-impregnated bread and milk or porridge. (2) The œsophagoscope is then used to confirm the diagnosis and explore the cancerous area as far as possible; for this a general anæsthetic is often desirable. (3) If the stricture is too tight to admit of the radium apparatus, it is sufficiently dilated up by graduated bougieing through the œsophagoscope, a procedure which can be carried out more thoroughly under a general anæsthetic. Should the stricture not be dilatable sufficiently to take the radium tube, the latter is passed down through the œsophagoscope as far as it will go and allowed to sit on the narrower part of the stricture.

The practice of œsophagoscopists have differed in matters of detail. Some insert the radium tube in a hollow gum elastic catheter and allow this to remain *in situ* for two or three hours or more. Others insert the radium tube through the endoscope into the stricture with slender forceps and allow it to be *held* in the stricture. The tube is enclosed in rubber as described in the special section dealing with radium in the pharynx (*q. v.*), string being attached to prevent displacement, to withdraw the apparatus at the end of the application or to draw it up to a higher portion of the stricture. This was the method followed by me in earlier cases, and it has the advantage over the styletted apparatus which Finzi and I have largely adopted during the last three years in that it causes less discomfort to the patient than when a style passes through the pharynx and is attached to the teeth. One of the advantages of the styletted apparatus is that it can be more speedily and accurately inserted under cocaine anæsthesia; and we have found it indispensable in our more recent practice of immediately checking the position of the apparatus by means of the X-rays and a bismuth meal. If the radium tube is seen on the screen to be not quite in position it can be

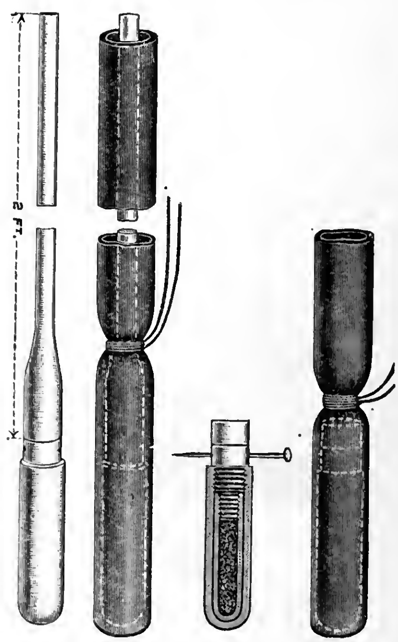


Fig. 18.—Finzi's apparatus with rubber covering.

accurately raised or lowered by means of the soft silver style. When this radiographic check is not used, one has to rely on very careful measurements made before inserting the tube, as to the depth from the teeth at which it is

to be inserted; this distance has to be carefully marked off on the style by a silk ligature. In long strictures the radium tube can be allowed to remain *in situ* in the lower part of the stricture for from eight to twelve hours and then pulled up the length of the tube for a further period into the upper part.

In conjunction with Finzi I have sometimes used two tubes arranged tandem and on one occasion we inserted three tubes thus arranged one above the other. Such a long stricture

FIG. 19.—Radium tube attached to a flexible silver style, which is inserted into a malignant stricture with the aid of Hills' œsophagoscopic tube; the lateral slot in the latter enables it to be withdrawn without disturbing the position of the radium apparatus.

is, however, usually unsuitable for radium treatment.

When the patient is intolerant to endoscopic manipulations the apparatus can be inserted under a general anæsthetic. This can be done at the initial examination when dilating up the stricture, but has the disadvantage that it cannot be carried out in the X-ray room in order to check the exact position of the apparatus; when the stricture is too tight after dilating up to admit of the passage of the tube through it there is, of course, no advantage in resorting to subsequent radiography.

As regards the length of exposure to the rays when using the amount usually employed, viz. 100 mg. of radium salt (measured as pure radium bromide) or its emanation equivalent, Guisez, who has had considerable experience, recommends in his book on *Diseases of the Œsophagus*, published in 1911, an application of four or five hours every other day until a total of twenty-four to thirty hours is attained. He uses silver screens amounting to $\frac{8}{10}$ of a millimetre in thickness enclosed in a gum elastic sound. Under the guidance of Finzi I have used screens of either silver, lead or platinum of from $1\frac{1}{2}$–$2\frac{1}{2}$ mm. in thickness enclosed in rubber 1 mm. thick. Our present practice for 100 mg. is to use a platinum screen, 2 mm. thick, enclosed in rubber and to allow the tube to remain at one spot for twelve hours at the lower part of a long stricture. If the apparatus is then raised, say 2 or 3 cm. to act on the upper part of the stricture, it can remain in another twelve hours, if the patient will tolerate it; if not, another application is made after an interval of two or three days. No fresh application is made earlier than six weeks—that is to say, after all reaction has passed off. This is in accordance with the practice of Dominici, and has been followed also by Knox and by Pinch. An œsophagoscopic examination is made before repeating the treatment. A second application is usually called for at the end of six weeks in cases where there is marked or moderate improvement; and subsequent applications are made according to local appearances. The treatment should not be persisted in when no very obvious good is effected.

If a thinner screen is used in tight strictures, and especially when a window-screen is employed in cancers, limited to a lateral segment of the tube of the gullet, then the exposure should not exceed six or eight hours on end.

There is rarely any difficulty in inducing the patient to tolerate the apparatus for twelve hours when it has been inserted under a general anæsthetic, as the drowsiness can be kept up by a judicious employment of morphia and atropine. The same sedatives, or else scopomorphine, are essential when the apparatus is inserted under cocaine anæsthesia. Some patients manage to swallow water fairly well with the styletted apparatus in position, but in other cases if thirst is complained of this should be relieved by the sucking of ice or of lemons. I have only on a few occasions kept the radium tube in position for such long periods as twenty-four and twenty-eight hours, but even then have not had recourse to rectal feeding. After removal of the apparatus more or less soreness behind the cricoid is usually complained of, but passes off in a few days and rarely increases dysphagia to a marked extent.

The contra-indications include an advanced stage of the disease with involvement of several inches of the gullet, the penetration of the

growth into the lumen of the trachea or bronchi, or invasion of the lungs, marked involvement of the glands of the neck or mediastinum, and lesions of the phreno-cardiac portion of the gullet with probable extension to the stomach. Patients who are greatly debilitated or who have undoubted cardiac weakness are unsuitable for the employment of either local or general anæsthesia and would be unable to tolerate the apparatus for a sufficiently long exposure. Chronic bronchitis I regard as another contra-indication in elderly and weak subjects. In fact, patients should be in fair general health and the strictured area should not be more than 5 or 6 cm. long. Fungation is not a contra-indication.

Diet.—The question of appropriate diet in various types of stricture is of great importance, but space does not admit of its adequate discussion. Milk, egg and milk, thickened soups, purées, minced tripe, calves' head and fat bacon, custards and ice-creams can usually be swallowed in intubated cases *beside* the tube; liquids only should be given *through* the tube. In some unintubated cases fish tends to stick more than well-masticated butcher's meat.

Alimentation by the Rectum.—Rectal feeding is a valuable temporary expedient in acute œsophagitis and ulcer—whether due to traumatic and escharotic causes or not—in rupture from vomiting, in the case of impacted foreign bodies where it is desired by rest to reduce tumefaction caused by unskilled efforts at removal and preparatory to resorting to œsophagoscopic measures, in some cases of carcinoma more especially to render the patient more fit for gastrostomy, and also to supplement alimentation *per vias naturales*, where swallowing is either difficult or painful. It is also usefully employed for two or three days after excisions of portions of the pharynx, larynx and œsophagus, where regurgitation and vomiting of food may soil the incised tissues before the lymphatics are sealed up.

The possibilities and limitations of rectal feeding is fully dealt with elsewhere, but it may be well to repeat here that Langdon Brown has shown that the nutrient enemata containing peptonised proteids, which have hitherto been so largely employed, have no nutritive value worth mentioning and are little superior in that respect to mere saline enemata which relieve thirst, increase the volume of blood in the vessels after hæmorrhage and are less messy and free from a tendency to decomposition. Proteins are not absorbed as peptones in the lower alimentary tract, but as amino-acids; peptonisation, therefore, does not go far enough to render proteid enemata absorbable by the lower bowel.

Pancreatised milk and dextrose form the best ingredients for nitrogenous rectal feeds. Rendle Short gives the following directions for their preparation: "To a pint and a half of milk boiled and cooled add ½ oz. of some reliable pancreatic fluid or four pancreatic tablets; keep in the incubator twenty-four hours; add ½ oz. of pure dextrose. Give 5 oz. every four hours, or if the patient can retain it 10 oz. every eight hours." Where the patient is very thirsty, whether from severe loss of blood, or otherwise, a saline enema can be given in the first instance and the nutrient injection resorted to later.

The Treatment of the Commoner Diseases of the Œsophagus

Neuroses of the Gullet.—Organic paralysis is not often met with, but when present is usually of central origin, *e. g.* hæmorrhage and tumours of the pons and medulla, bulbar paralysis, multiple sclerosis, locomotor ataxy, general paralysis of the insane, and, in short, in any lesion affecting the deglutition centre. The use of a feeding-tube is necessary in advanced cases, and beyond this local treatment, *e. g.* electricity, is of little value. The latter, however, may be tried in the form of sinusoidal current in those rare cases of peripheral neuritis of the plexus gulae occurring after, *e.g.* diphtheria and influenza. For general constitutional treatment the section on *Disorders of the Nervous System* can be consulted.

Spasmodic Paroxysms may occur in association with pharyngeal spasm as a symptom of certain general diseases such as rabies, tetanus, epilepsy, chorea, strychnine poisoning and hysteria; the appropriate treatment for which is dealt with elsewhere. Primary *functional spasm* is usually, but probably erroneously, held to be a common cause of intermittent dysphagia. Painful colic is the characteristic mark of spasm in the intestinal tract, and unless this is present the diagnosis of spasm is almost certainly unwarranted, and when present the colic is almost invariably *secondary* to an organic lesion of the gullet. True functional dysphagia is usually painless and due to paresis rather than to primary, *i. e.* idiopathic, spasm.

In functional paresis bougieing has a stimulating effect in some cases, and this can be reinforced by the intra-œsophageal employment of the sinusoidal current. The treatment of secondary spasm consists in relieving the cause which is generally of the nature of acute or subacute inflammation causing stenosis or is due to the presence of a well-established organic stricture. The use of the bougie relieves by reducing the stenosis. A number of conditions have been inaccurately grouped together under the heading of primary cardiospasm. Gottstein mentions the following: (1) kinking or angulation of the

lower or phreno-cardiac portion of the œsophagus; (2) congenital defects; (3) atony, *i. e.* paresis, either fundamental or organic; (4) œsophagitis with temporary or permanent anatomic narrowing near the cardia; (5) genuine cardiospasm. In my experience either paresis, angulation, tumefactive œsophagitis, or a permanent anatomic stricture are the conditions found on œsophagoscopic examination, and for these the term cardiospasm is a misnomer. The above conditions are relieved by bougieing which would only induce and aggravate primary spasm.

Acute Œsophagitis.—This probably is never primary, but secondary to acute stomatitis, to septic pharyngitis, to thrush, to gastritis, or to continued bilious vomiting (two cases seen by the writer); it may be symptomatic, as in impaction of foreign bodies, in traumatic and escharotic œsophagitis and in ulceration from typhoid fever, smallpox and diphtheria, and in peptic ulcers near the cardia. There is often fever, and nearly always burning pain, aggravated by swallowing, which latter is difficult. Stiffness and tenderness to pressure in the neck, profuse salivation and expectoration of frothy mucus were constant symptoms in the few recorded cases. The absence of marked attacks of spontaneous spasms in the pharynx and neck distinguishes it from hydrophobia, but it is not always possible to exclude deep peri-œsophageal abscess even by œsophagoscopy. Ice, cocaine and chloretone locally, and morphia and atropine hypodermically, abstinence from food by the mouth for a day or two and the administration of saline rectal injections may give relief. Feeding through a stomach tube, or the wearing temporarily of an intubation apparatus, is indicated where swallowing is extremely difficult and painful, and more especially if there is ulceration, provided that the wearing the tube does not itself cause much pain. The general constitutional treatment depends on the cause. In septic cases with fever, autogenous vaccines are indicated.

Fibrous Stricture of the Gullet.—This may result from any condition causing ulceration, for example, traumatism from unskilful instrumentation, ulceration resulting from impacted foreign bodies, from swallowing corrosive fluids, from syphilitic lesions, and also from general hypertrophic thickening in the phreno-cardiac portion of the gullet; the latter is usually obscure in origin, but may have been preceded by definite œsophagitis due to diphtheritic lesions or to peptic ulcers in association with gastritis. I have never known primary spasm to be the cause. Dysphagia is the most prominent symptom, with regurgitation of food, the amount and character of which varies with the degree and site of the superimposed dilatations; œsophagoscopic measures will determine the site, degree and nature of the stricture; the amount of dilatation above, and the length of the stricture being best shown by radiography in conjunction with a bismuth meal. When resulting from the swallowing of corrosive fluids the stricture may be so long and tight that endoscopic dilatation by bougies may be useless and gastrostomy may then be unavoidable; in most cases, however, endoscopic dilatation by bougies and reinforced in some cases by the employment of Brünings' or Abrand's dilator, followed by temporary intubation, will afford relief for months or years, when these measures may have to be repeated.

Internal œsophagotomy performed through the endoscope is rarely advisable or called for, is not free from danger, and is applicable only to very short, tight annular strictures. External cervical œsophagotomy is practically an obsolete method, and is more dangerous and less convenient for the patient than gastrostomy. In tight strictures of the phreno-cardiac region, gastrostomy can be supplemented by digital dilation and followed by tubage.

Lavage of the dilated gullet is always useful, especially where there has been erosion from continuous retention of decomposing foreign matter. Mercury and iodide of potassium are, of course, indicated in syphilitic cases, but such measures as fibrolysin injections and ionisation are probably not worth the trouble involved in their employment. The measures to be relied on are dilating up with bougies through the œsophagoscope followed by continuous dilation for a week or two by wearing an intubation apparatus. This treatment may have to be repeated periodically. Stretching the strictures by expanding metal dilators and by pneumatic and hydrostatic bags is rarely either necessary or advisable.

Dilatations of the Œsophagus.—A general ectasia of the gullet occurs above any stricture which is of long duration, *e. g.* in cicatricial stricture, in long-impacted foreign bodies, and in cancer. Congenital, idiopathic and spasmodic dilatations are described, but the evidence of their existence is, in the writer's experience, unconvincing. In diffuse dilatation, when no anatomic narrowing of the phreno-cardiac gullet exists, the explanation is probably to be found either in angulation, kinking or in general paresis of the gullet, with want of co-ordination of the act of deglutition, the cardia not opening up normally; the latter is better explained by paresis than by hypertonic spasm. True dilatations are usually either fusiform or globular, but in carcinomatous stricture the lower part of the ectasia may appear irregular in the X-ray photograph after a bismuth paste meal. Dilatations of the gullet are often

associated with regurgitation (œsophageal vomiting). Palliative treatment consists in dealing with any stricture by dilatation, and with the paresis, if present, by lavage and the employment of the sinusoidal current. Ordinary galvanism is dangerous in unskilled hands.

Malignant Stricture of the Œsophagus. — Epithelioma is the commonest form, but spheroidal-celled carcinoma and endothelial sarcomas are met with; colloid cancer and true sarcomas are very exceptional. The disease may originate in any portion of the tube, but the constriction at the entrance to the gullet, opposite the left bronchus, and at the phrenic constriction, where the tube passes through the diaphragm, and at the cardiac orifice are the favourite sites. The *revealing signs* of malignant stricture are late; *slight* dysphagia is the earliest symptom; and this often appears suddenly, as after a piece of meat becoming impacted, the patient never afterwards being free from slight difficulty with solids, though liquids may pass freely for a time; the dysphagia is usually progressive and rarely intermittent; it may never interfere with the patient taking sufficient nourishment *per vias naturales ;* on the other hand, complete aphagia may ensue, necessitating intubation or gastrostomy. By radiography we can observe the level of the upper and lower ends of the stricture and its calibre to a certain extent, and also the amount of dilatation above the stricture, but it is only by a direct œsophagoscopic examination that the nature of the stricture can be determined with anything approaching certainty. This should always be resorted to; the writer has found on six occasions that the diagnosis of cancer, which was made by others, and seemed to be justified on clinical grounds, had to be abandoned after an endoscopic inspection had shown the stricture to be non-malignant and therefore amenable to endo-œsophageal treatment. The endoscopic inspection should also include an examination of the larynx, trachea and bronchi, as extension to these areas, before there are any obvious pulmonary symptoms, should influence not only the prognosis, but also the treatment for such conditions; for if the air tubes are invaded the employment of radium, for instance, is contra-indicated, and intubation methods are especially suitable.

The treatment of primary gullet cancer is practically always merely palliative for the relief of dysphagia and pain. The only cases in which operation has hitherto been successful were in all probability not instances of primary disease, but of invasion cancer from the pharynx, and in these instances Solis Cohen's and Gluck's types of operation, viz. total laryngectomy together with partial excision of the deep pharynx and a small segment of the adjacent cervical œsophagus, have often been successful; when the larynx, the posterior surface of the cricoid plate and the pyriform fossæ are free from disease the larynx need not be removed. The technique is well described by Trotter in his recent Hunterian Lectures. Œsophagectomy alone, whether of the cervical œsophagus as first practised by Czerny, or of the thoracic, or of the abdomino-thoracic œsophagus by thoracotomy after the methods of Sauerbruch, von Hacker, W. Meyer and others, had until recently no permanent or even temporary cure to its credit. In 1913, however, Torek, of New York, removed a portion of the thoracic gullet for cancer, with survival of the patient after an extensive posterior thoracotomy; and another operative survival has lately been reported. With early recognition by means of the more general adoption of exact endoscopic methods of diagnosis with the œsophago-gastroscope, together with improvements in operative technique, an occasional successful œsophagectomy may be expected.

Killian has claimed to have diagnosed and successfully removed a small sarcoma of the gullet by endo-œsophageal measures through the œsophagoscope, but it will probably be long before another such cure is recorded.

Palliative gastrostomy is the only external operation extensively practised; with the more general resort to intubation rendered possible by the recent adoption of endoscopic methods, the number of cases gastrostomised should be largely reduced. It is specially indicated where intubation is often too dangerous or impossible, as in long, tight strictures, more especially in the phreno-cardiac region. Gastrostomy should not be put off till the patient is in a thoroughly debilitated condition; on the other hand, some surgeons, in the writer's opinion, resort to gastrostomy at too early a stage, when intubation and other measures, if œsophagoscopically carried out would be quite sufficient for the comfort of the patient.

Iodides, iodipin, fibrolysin, like serums, vaccines and enzymes, are not often even of temporary value. Some measure of success has been claimed for colloidal preparations of selenium and of copper. Of drugs acting locally spirit of ether breaks up frothy mucus in the gullet by reducing surface tension. Astringents, like adrenalin, cocaine and turpentine, are of little use; local anodynes, such as morphia, chloretone and orthoform, combined with bismuth emulsion are sometimes useful for pain in cancer high up; they rarely, however, enable one to dispense with hypodermic injections of morphia, atropine, etc., in very painful cases.

Lavage of the gullet, in cases of dilatation

above a stricture, is the best means of removing decomposing substances, such as food residues and the products of ulceration, but glycerine of boric acid and of carbolic acid, sanitas and similar preparations are also useful as disinfectants and deodorants. Peroxide of hydrogen is contra-indicated as it may cause respiratory embarrassment.

Caustics are generally inadvisable, even when applied endoscopically to tight strictures and diathermy; ionisation and carbon dioxide snow have not as yet had any extensive trial. Relief of dysphagia by X-rays has been claimed in a few instances.

Blind use of bougies undoubtedly gives relief to dysphagia, but is not free from danger even in expert hands, and should be abandoned in favour of endoscopic bougieing, which is a much safer and more efficient procedure in every way—but with intubation periodical bougieing is unnecessary.

Symonds' gum elastic funnels are extremely useful when the gullet can be endoscopically dilated up to a sufficient size to permit of their insertion. They are especially indicated in perforation into the air passages, but cannot be used in stricture near either end of the gullet. Berry's and Symonds' rubber tubes are also useful, but have been largely superseded after much experience by the writer in favour of his styletted oro-œsophago-gastric tube, which can be fastened to the teeth and retained temporarily or permanently without any fear of being coughed or vomited up; it is inserted through the œsophagoscope after dilating up the stricture. The patient is first of all fed with liquids by a funnel through the tube, but later liquids and frequently solids pass readily by the side of the tube owing to the continuous bougie effect on the stricture. This form of intubation apparatus is equally suitable for cases when the stricture is at the entrance to the gullet or well in the thorax; it must, however, be passed with caution in malignant stricture of the phreno-cardiac portion of the œsophagus, as the gullet here takes a curve forward and to the left, and the lesser sac of the peritoneum has been more than once perforated by instrumentation in this region.

The most recent and probably the most valuable palliative measure which has been employed in cancer of the gullet is the application of radium salts or of radium emanation suitably screened. The remedy is like most therapeutic procedures, an uncertain one, but where the disease is not very extensive, the radium tube can be accurately inserted into the stricture by means of the œsophagoscope aided by the X-ray screen, and the results, though probably only temporary, are certainly often most effectual, not only in causing subjective relief of symptoms and temporary cessation of the dysphagia and expectoration, but also in bringing about widening of lumen, healing of ulcers, and sometimes even leading to the temporary disappearance of all naked-eye objective evidence of disease. The writer has employed this method in conjunction with Finzi in over thirty cases of gullet cancer, using from 50 to 200 mg. of radium salt screened in lead, silver or platinum of from $1\frac{1}{2}$ to $2\frac{1}{2}$ mm. in thickness, and in more than half the number there was either remarkable or very substantial improvement. [See pp. 281–284.]

W. H.

DISEASES OF THE STOMACH

The basis of the rational treatment of diseases of the stomach is the proper conception of the disturbances of functional activity which therein obtain, and the capacity of our therapeutic measures to restore these to normal limits.

Disturbances of functional activity are immediately responsible for the subjective manifestations of gastric disorder, the phenomena which obtrude themselves unpleasantly upon the consciousness of the individual, and they may or may not be associated with, and dependent upon, some structural change in the organ. On the other hand, it is highly probable that any structural change will remain subjectively latent unless it is associated with a perversion of functional activity beyond the normal limits.

In medical treatment, our therapeutic measures are directed immediately to the restoration of such disordered function, and very remotely to the reparation of any morbid structural change, and that only by neutralising or removing such conditions as conceivably interfere with natural reparative processes.

Dyspepsia.—It is convenient to employ this term to comprehend the subjective manifestations of all the various perversions of gastric functional activity, however arising, rather than to limit it to any particular types of doubtful origin.

Dyspepsia may be of a (1) *Simple Type*—depending wholly upon a lack of correlation between the digestive requirements of the ingesta and the functional capacity of the stomach.

(2) *Reflex Type*—depending upon the existence of some lesion more or less remote from the stomach, and a more or less susceptible nervous reflex mechanism.

(3) *Organic Type*—depending upon some structural change in the stomach itself.

With a view to treatment, it is necessary at the outset to determine to which of these types any case of gastric disorder belongs.

Simple Dyspepsia

This condition depending upon either the dietetic abuse of a normal gastric mechanism or of one enfeebled by some general or constitutional condition, by anomalies in the quantity or quality of food, its preparation, its mastication or its ingestion, demands a careful correlation of the diet and the functional capacity of the stomach as the essential factor in its treatment.

In all cases the mouth and teeth should be carefully examined, and any defects in the number or relations of the teeth, painful caries and pyorrhœa, should be remedied.

It is useful to get the individual to relate in detail the diet of one or two typical days, noting times of meals, the length of time given to them, the doings of the individual immediately before and after meals, the kind and amount of food taken. In this way it is generally possible to determine the essential factors in the dyspeptic disturbance. Arriving at meals in a physically or mentally exhausted condition, immediately leaving for further strenuous occupation, "bolting" food in an imperfectly masticated condition, the taking of "nips" of alcohol or too-frequent "appetisers," of excessive quantities of tea or coffee, of rich, highly seasoned foods, of made dishes, or of foods recognisedly difficult of digestion, or the abuse of tobacco. The re-ordering of the daily life of the individual, insisting upon regularity of meal-times, adequate rest before and after meals, thorough mastication, the substitution of simple, plainly cooked foods for made dishes and indigestible viands, cutting down the starchy foods, the substitution of split toast and crust for bread and potatoes, the elimination of alcohol and coffee and of tea and tobacco in excess, generally suffice to put an end to the dyspepsia. The difficulties of treatment are often found to be not in the measures to be employed as in persuading the individual to carry them out.

Should symptoms of gastric irritability still persist after the reorganisation of the diet, these may be met by the administration of takadiastase immediately after food, and of a simple bismuth and soda mixture some ten or fifteen minutes later.

A more severe type, which in its most developed form constitutes a variety of the so-called nervous dyspepsia, is associated with the nervous exhaustion entailed by mental worry, sexual excess, etc. It calls for a very strict supervision of the daily life of the individual, a complete rest at some quiet inland resort, preferably of a fairly high altitude, a course of physical exercises, or of massage, and the administration of bromides along with bismuth and soda after food.

The second variety of simple dyspepsia, *atonic, asthenic or myasthenic dyspepsia*, depends on a perversion of the functional activity of the stomach associated with and secondary to some general or constitutional condition, exhausting illnesses, anæmia, constipation (cæcal stagnation) neurasthenia, constitutional asthenia (Stiller). The disordered functional activity chiefly concerns the motor functions of the stomach, viz. deficient tonic contraction of the body (peristole); the peristaltic activity of the pyloric portion, on the other hand, shows curious variations, periods of normal or excessive activity with spasm alternating with periods of deficiency in which stagnation occurs. The secretory activity of the stomach also varies, in most cases it is about the lower normal limits, in some it is somewhat above normal, in a few it is considerably depressed.

In the treatment of this variety the general condition must be actively dealt with, and an improvement in the general nutrition is invariably indicated; this has to be met by such careful regulation of the dietary as will provide the greatest possible nutrition with the least strain on the stomach. In severe cases, and even in slight cases where possible, the patient should be confined to bed, or at least the horizontal position should be assumed for half an hour or more after each meal. In this way much strain is taken off the stomach, and its emptying facilitated. Washing out the stomach last thing at night with warm normal saline is of advantage when there is stagnation, in so far as it ensures a few hours' absolute rest for the stomach. Abdominal massage each day, and general massage two or three times a week, should be employed to improve the tone of the stomach and the general condition. The diet should be divided into four or even five small meals a day, and should consist of junket, custard, jellies, lightly cooked eggs, stewed tripe, steamed white fish, chicken, pigeons, lightly grilled and minced beef or mutton, purée of potato in small quantities, spinach, turnip-tops, split toast, crust, rusks, well-cooked sago, etc. The food should thus be semi-solid in character, and the amount of fat restricted, owing to its inhibitory action on gastric motility. Of fluids, two small cups of weak tea may be allowed, but coffee and cocoa should be avoided; in addition, the patient should take half a pint of hot water each morning, to which may be added a teaspoonful of Carlsbad salts if the bowels are constipated. Of drugs, strychnine is most generally employed for its reputed action in improving the motility of the stomach, and it may be administered in combination with dilute hydrochloric acid (20 min.) after food, in those cases where the secretory activity is also deficient,

ɪr as Tinct. Nuc. Vom. with Sod. Bicarb. and ĭod. Brom., where the secretion is excessive.

Physostigmine also exerts a stimulating action n the gastric musculature, and may be given a doses of $\frac{1}{100}$ gr. once or twice a day. Should he bowels be obstinately constipated, simple oap and water enemata and petroleum are ɪreferable to powerful aperients.

Subsequently the patient should endeavour o maintain an improved general condition by egulated physical exercises.

Reflex Dyspepsia

The gastric functions may be disordered eflexly by a lesion situated more or less emote from the stomach itself. The two ssential factors in the production of this ondition are the existence of such a lesion and n increased susceptibility of the reflex nervous nechanism. These may vary indirectly, thus ome lesions, as a duodenal ulcer, may assert heir existence through a nervous mechanism ttle more susceptible than the normal; whilst thers, as some ileo-cæcal lesions, may remain ıtent until the susceptibility becomes greatly xaggerated. There is little doubt that many ıch cases were formerly classed as nervous yspepsia. The chief lesions are: duodenal lcer, cholecystitis, chronic appendicular lesions, eal kinks, chronic ileo-cæcal inflammations, æcal and colonic stagnation, diseases of the enerative organs in females, mobility of the idneys, diseases of the central nervous system.

In such conditions the objective of medical reatment is to counteract or neutralise the ınctional disturbance in the stomach, to epress the susceptibility of the reflex nervous nechanism, and to establish such conditions s will be favourable to the resolution or uiescence of the maintaining lesion. Complete nd permanent relief of the reflex gastric isorder often calls for operative intervention or the eradication of the responsible lesion, ut even in this latter contingency it is well to emember that with a nervous mechanism ufficiently unstable, the healing process followıg operation may suffice to maintain some egree of gastric disorder.

The particular disorder of functional activity 'hich characterises this type consists in exessive activity, both of the secretory and the notor functions of the stomach—the so-called ypersthenic dyspepsia, or *acid dyspepsia* ıcluding *hyperchlorhydria, hypersecretion*, alinentary and continuous, and gastrospasm and ylorospasm, all of which are, in all probability, arying degrees of one and the same type of ınctional disturbance.

The peculiar intermittency which characterises this type of dyspepsia depends in some cases n the varying susceptibility of the reflex nervous mechanism, in others on exacerbations of the lesion responsible; in the former it is usual to find that the dyspeptic disturbance disappears when the individual is removed from some enervating influence, as during a holiday.

The treatment of this type of gastric disorder is rapidly approaching the realm of rational therapeutics. The empirical use of alkalies in the treatment of dyspepsia generally has been attended with success in the majority of cases because they are of this type, and alkalies acting simply as neutralising agents counteract the excessive acidity of the stomach contents and so remove a potent factor in the production of the subjective discomfort. There is no evidence that the administration of alkalies before food exerts any stimulating effect on gastric secretion, as was formerly believed. A large draught of warm alkaline fluid may undoubtedly be beneficial as a cleansing agent in cases of catarrhal gastritis where the gastric mucosa is covered by a layer of mucus, and so get rid of a material which would utilise some of the digestive activity of the gastric juice secreted. On the other hand, alkalies administered during digestion act solely as neutralising agents, combining with the acid of the stomach contents, but effecting no alteration in the actual secretion of the gastric juice itself unless given in large quantities and for long periods, when a temporary depression of secretion has been produced. Since in reflex dyspepsia excessive secretion and excessively prolonged secretion of gastric juice are, in varying degrees, constant factors, the administration of alkalies during digestion is called for to neutralise the excessive acidity of the stomach contents. Of the various alkalies which may be employed the bicarbonate of soda, the carbonates of bismuth, magnesia and lime, and the oxide of magnesia, are the most useful. The action of the soluble bicarbonate of soda is rapid and ephemeral, that of the insoluble carbonates of the heavy metals is more prolonged. Bismuth possibly exerts some sedative action on the gastric mucosa; it is, moreover, constipating. Magnesia, on being converted into the chloride, exerts a laxative effect, accordingly varying combinations of the salts of bismuth and magnesia are efficient in neutralising the excessive acid of the stomach contents and in regulating the activity of the bowels.

The excessive secretory activity is associated with some perversion of the motility of the stomach, excessive peristalsis of the pyloric portion leading in many instances to rapid emptying of the stomach, and quite commonly to painful cramp-like spasms of the pyloric mechanism; the concentric tonic contraction of the body of the stomach—peristole—is also as a rule excessive, but with periods of relative

atony. As these perversions of motility are probably a direct effect of the excessive secretion, the neutralising effect of alkalies influences beneficially the disordered motility by removing the stimulus to its production. Belladonna exerts a direct inhibitory effect on the secretion of gastric juice as it does on the secretion of saliva, and further, it has the power of relaxing spasm of the gastric musculature; accordingly, the exhibition of this drug is indicated whenever there is excessive gastric activity; it is interesting to note that its action differs from that of alkalies in that it inhibits excessive reaction of the stomach to the stimulus to secretion, whereas alkalies merely neutralise the product of such excessive activity.

Neutral fats, as olive oil, oil of sweet almonds, fresh butter, cream, also exert an inhibitory effect on gastric secretion, and at the same time an inhibitory effect on gastric peristalsis, and so a meal taken within half an hour of the administration of half to one ounce of such a neutral fat on the fasting stomach passes into the duodenum more slowly, and partly by inhibition and partly by dilution, the acidity of the stomach contents is greatly reduced. It is evident, then, that in the alkalies, belladonna and neutral fats, we have the means by which the disordered functional activity of the stomach in reflex dyspepsia can be neutralised and counteracted, and by their rational use the subjective discomfort can be completely ameliorated, even the severe pain associated with pyloric and other forms of gastric spasm. The use of morphia, on the other hand, in such conditions is contra-indicated by the fact that it is a stimulant of gastric secretion, and while dulling the sensorium to the discomfort, exaggerates the local disorder from which that discomfort arises.

The drug treatment of reflex dyspepsia may be summarised as consisting in the administration of the alkaline salts of bismuth and magnesia in such quantity and combination as will neutralise the excessive acidity of the stomach contents and at the same time regulate the bowels, and of belladonna in doses of 5 min. of the tincture. These may be combined and given ten to fifteen minutes after food, the alkaline salts by their weight remaining in the stomach, and by their relatively slow action gradually neutralising the excess of acid as it is secreted; the belladonna also will have sufficient time in which to produce its inhibitory effect when most required, at the maximum phase of digestion.

To depress the reflex activity of the local nervous mechanism, a further indication in the treatment of this type of dyspepsia, the administration of bromides is called for, and either the potassium or sodium salt may be combined with the above. With this object also it is often essential that the individual should be removed from all enervating influences, as business and other worries, and in severe cases it is advisable to insist on a period of absolute rest in bed of at least a month.

The diet is equally important; there are certain foodstuffs which must be rigorously excluded by reason of their uselessly stimulating effect on gastric secretion—viz. coffee, strong tea, meat extracts, alcohol (unless very dilute), malt liquors, fried foods, especially starches cooked with fat, as pastry, fried bread, hot buttered toast, etc., stewed meats and highly seasoned foods. The amount of starchy food must be reduced, and what starch is allowed should be partially dextrinised, as in split toast, breakfast biscuits, rusks, crust.

Milk, cream, butter (cold), junket, eggs (raw or lightly cooked), custard, plainly cooked meats, steamed white fish—as plaice, sole, hake, birds boiled or plainly cooked in a casserole, grilled lean beef or mutton or plainly roast, purée of potato in small amount, of spinach or of turnip-tops, or French beans, two small cups of weak tea per day, provide the menu from which a suitable and varied diet may be selected.

Should the symptoms of dyspepsia persist with this régime, particularly should these be characterised by such manifestations of hyperacidity as heartburn, acid risings, etc., then the particular effect of the neutral fats may be utilised by the administration of olive oil or oil of sweet almonds in doses of half to one ounce half an hour before meals.

Organic Dyspepsia

Gastritis.—The indications for treatment are to remove the irritant responsible for the condition, and to aid in the restoration of the organ to the greatest possible anatomical and physiological integrity.

Acute Gastritis.—A condition of very diverse intensity, due to the local action of various irritant substances, calls for the immediate removal or neutralisation of the noxious substance and a variable period of physiological rest for the inflamed organ. The removal of the noxious substance is partly or wholly achieved by the vomiting which naturally occurs, and in such cases the only question to be decided is how far this shall be artificially modified. In any case seen in the early stage vomiting should be encouraged and its efficacy increased by the administration of warm water and irritation of the fauces if necessary, in children and strong adults the cleansing of the stomach may be initiated or accelerated by the simultaneous administration of some such emetic as zinc sulphate or vinum ipecacuanhæ, or by the passage of a soft stomach tube and lavage,

ut neither of these procedures should be emloyed where the inflammation is of the destrucive type produced by corrosive poisons, and in uch cases removal of the causal agent must be ttempted by dilution and neutralisation only.

The patient should then be placed in bed, ie extremities kept warm, and light fomentaons should be applied over the epigastrium t first with some such counter-irritant as urpentine or mustard until the skin is deeply ddened but not blistered. The mouth and eeth should be carefully cleansed with an lkaline antiseptic mouth-wash, and the patient hould be allowed to take cold water (iced) by ie mouth in teaspoonfuls every half hour. o attempt to administer any food should be nade for from twelve to thirty-six hours, ccording to the severity of the condition. Vhere the administration of water by the mouth s above induces retching, or where from the verity of the condition it is obvious that the omach must be kept absolutely at rest, ater should be administered by the rectum. fter a preliminary cleansing enema the atient should receive from ten to fifteen unces of normal saline at a temperature of 00° F., run slowly into the rectum from a innel and a rectal tube every four or six hours, r oftener should it be well retained and the ongue is at all tending to dryness. When ie condition is associated with marked restssness or when retching still continues, it is seful to add to every other saline, sodium romide in doses of from three to five grains o the ounce. Where the gastritis is associated ith severe enteritis and diarrhœa, severe epletion and collapse must be met by the xhibition of normal saline either subcutaneously r intravenously. When it appears that the dministration of water by the mouth causes o discomfort, it may be gradually replaced y whey, albumen water, and then milk, iluted with water, lime-water or soda-water, r citrated effervescent water as citoda, or ven weak tea without milk or sugar, which to nany patients is peculiarly refreshing. From iluted milk, the patient should be allowed such land foods as Benger's, Mellin's, Allenbury's, ago milk, rice milk, with rusks, and later junket, ustard, jellies, meat broths, and so gradually o a light diet of chicken and fish. Drugs may ot be required at all; on the other hand, it is enerally advisable to provide for thorough vacuation of the bowels by the early adninistration of ½ oz. castor oil with tincture f opium in 10 min. doses, or of calomel gr. every hour until the bowels act. When he administration of food is associated with iscomfort or a tendency to vomit, this may be net by the administration of either milk of nagnesia, with some carminative as spirits of chloroform or of a simple mixture of bismuth carbonate 10 gr., sodium bicarbonate 15 gr., sodium bromide 5 gr., in peppermint water, after food. Persistent retching, which occasionally occurs, can be relieved by cocaine in doses of ¼ gr. in a teaspoonful of water, given at intervals of an hour.

Collapse must be met by the administration of strychnine subcutaneously or brandy per rectum, in addition to the measures above indicated.

Chronic Gastritis.—Chronic gastric catarrh. These terms have been applied to various disorders of the stomach which have no relation in fact with chronic inflammation of the gastric mucosa. Genuine chronic gastritis in a degree to give rise to any recognisable subjective manifestations is a comparatively rare condition, and certainly very much less frequent than would appear from the frequency with which its existence is diagnosed. A conspicuous and characteristic feature of chronic gastritis is the presence of an abnormally large amount of mucus in the stomach contents, and occasionally it happens that this increased secretion of mucus is so considerable that the term *gastromyxorrhœa* has been applied to what is probably a variety of chronic gastritis. The secretory activity of the stomach in chronic gastritis shows considerable variations, in some there is hypersecretion, in others the secretion is normal, and again in others, and probably the majority, there is hyposecretion.

Treatment.—To avoid further irritation of the stomach the hygiene of the mouth, the method of mastication, and the diet must be carefully supervised. Carious and painful teeth, painful tooth-plates, pyorrhœa, must be looked for and put in order, faulty habits of mastication must be corrected. From the diet all irritating substances must be excluded, as alcohol, strong coffee and tea, spices and condiments, all highly seasoned and richly cooked foods, sweets, and the use of tobacco or other narcotic strictly regulated. The diet should consist of clear meat or vegetable soups, white fish steamed or boiled, plainly cooked meats, stewed tripe, chicken, grilled beef or mutton, green vegetable and potato in small amount in purée form, custard, junket, jellies, stewed fruits; split toast, thin stale bread, crust, rusks, butter, lightly cooked eggs, milk, plain or diluted with soda-water, lime-water, or citrated weak tea, and such alkaline waters as Evian, Vichy, Apollinaris, etc.

The excessive secretion of mucus must be dealt with either by systematic lavage or by large draughts of alkaline water. In severe cases the fasting stomach should be washed out each morning with an alkaline saline solution, as warm Vichy water or plain water,

to which a teaspoonful each of common salt and sodium bicarbonate have been added to each pint. If actual lavage is not employed, half a pint of hot Vichy water should be taken each morning.

All such cases derive considerable benefit from the routine treatment as carried out at various Continental spas, Homburg, Wiesbaden, Kissingen, in cases with hyposecretion; Carlsbad, Marienbad, Neuenahr, Vichy, Ems, etc., in cases with hypersecretion, where thorough lavage, either simple or in the form of a spray douche, is systematically carried out, and where diet and exercise can be more strictly supervised.

Of drugs, alkalies with bitters administered before meals are most useful. As sodium bicarbonate 15 gr., tincture of nux vomica 5 min., with infusion of gentian or condurango bark. In cases where there is manifest hyposecretion, this deficiency may be partially met by the administration of dilute hydrochloric acid after food, in combination with strychnine and quinine.

In many cases, especially where there is hypersecretion, there is an associated hepatic insufficiency, which appears to be benefited by small doses of Hyd. cum Cret. and Pulv. Rhei Co., each night, followed by a large draught of some alkaline saline aperient each morning.

Achylia Gastrica.—It is very probable that this condition of more or less complete deficiency of secretory activity depends upon chronic inflammatory changes in the gastric mucosa. Where the secretory activity of the stomach is so deficient as practically to exclude that organ from any digestive rôle, the obvious objectives of treatment must be to maintain the integrity of musculature of the stomach and to prevent stagnation. The diet should consist of such foods as remain in the stomach but a short time, and easily pass into the duodenum. Thoroughly cooked starchy foods, as rice, sago, tapioca, prepared oats, crust, breakfast biscuits, rusks, purée of potato, peas, beans, lentils, spinach, etc., may be allowed; of meats the most suitable are white fish, plaice, sole, hake, boiled or steamed, chicken, pigeon, pheasant and lamb, beef and veal, plainly cooked and minced, also tripe, cow-heel, calves'-feet and calves'-foot and meat jellies. Eggs in any form are to be excluded. Also the amount of fat as in milk, cream and butter should be somewhat curtailed. Of fluids, weak tea, aerated waters, and a little dilute claret may be allowed.

Any excessive secretion of mucus or any tendency to stagnation must be met by systematic lavage.

Of drugs the administration of dilute hydrochloric acid in doses of half a drachm well diluted after meals, together with strychnine and quinine, is most beneficial, by reason of their stimulating action on the gastric musculature, their antiseptic action, and the chemical action of the acid on the albumins. Hydrochloric acid may also be administered in a form with slower and more prolonged action as betain hydrochloride (acidol), which slowly decomposes in the stomach with the liberation of hydrochloric acid; the tablets in which form this substance is put up should be crushed before administration. Pepsin may also be given, along with hydrochloric acid or with acidol (acidol-pepsin).

Various preparations of the gastric juice of animals, as gasterine (dog), dyspeptine (pig), have been extensively tried, but with no very encouraging degree of success.

The general condition of the individual will also call for active treatment.

Gastric Ulcer.—The indications are to bring the stomach into such condition as will be most favourable to the complete resolution of the lesion, and to meet such incidental complications as may threaten the life of the individual. The situation of the lesion in the actively contractile wall of a viscus, the use of which is necessary to the nutrition of the individual, by precluding the possibility of visual inspection of the healing process, renders medical treatment peculiarly difficult and uncertain; and although gastric surgery has afforded abundant evidence that such lesions do soundly heal when the local conditions are made favourable, yet in the absence of actual inspection it is not possible to be certain in any case that the healing process has progressed sufficiently far as to warrant the individual safely assuming an ordinary mode of life. The disappearance of subjective and objective manifestations is no certain criterion, and even if the difficulty of maintaining any rigid system of treatment thereafter is overcome it is entirely a matter of speculation as to how long this should be maintained. The recurrence of manifestations some time after an apparently successful rest-cure is due in the majority of cases to the breaking down of an ulcer incompletely healed. The experiences of gastric surgery throw some light on the possibilities of the treatment of gastric ulcer by simple rest. After an operation involving section of the stomach wall it is common practice to allow food into the stomach on the second or third day, and a light but fairly complex diet by the end of the second week; from this it may be inferred that when a recent acute ulcer or erosion is so placed at rest that by contraction of the stomach wall its edges are brought into contact, it will heal rapidly and soundly; and further, that the factors which so obstinately militate against the sound healing of a chronic ulcer reside, not

in any conditions of the stomach as a whole or in any general condition of the individual, but in the ulcer itself, and, in fact, in the dense cicatricial base of the ulcer which admits only of such limited contraction that even with the stomach completely at rest the edges are far from being approximated. Under such conditions it is obvious that sound reparation of a large callous ulcer of the stomach must be a very prolonged process, and one which if incomplete must be fraught with the certainty of breaking down at an earlier or later period. It is thus evident that whilst the outlook for medical treatment is good in acute ulcer, it is but a temporary expedient in chronic ulcer, and any certainty of complete relief must be based on a much more prolonged régime than is usually practised.

From the therapeutic standpoint cases of ulcer of the stomach may be divided into—

1. Those in which perforation has occurred into the peritoneal cavity or into adhesions.

2. Those in which a manifest hæmorrhage has just occurred.

3. Those in which the manifestations do not include perforation, manifest hæmorrhage or mechanical disability of the stomach.

1. *Perforation.*—The existence of perforation is an absolute indication for immediate surgical intervention. Although there can be no doubt that minute leaking perforations do occur and heal with the formation of perigastric adhesions, yet in no circumstances, except where conceivably operation itself is the greater risk, should immediate surgical intervention be withheld.

2. *Hæmorrhage.*—Manifest hæmorrhage from the stomach or duodenum, whatever its presumable origin, must be met by rigidly confining the patient to bed, not allowing him to get up for micturition or defæcation, the head being kept low to obviate faintness. The mouth and teeth must be carefully cleansed with some alkaline antiseptic lotion, the colon cleared out with a large soap-and-water enema. An ice-bag slung from the frame of a bed-cradle should rest lightly on the epigastrium. The patient should then receive normal saline solution by the rectum, and nothing whatever, not even ice, by the mouth. The saline should be administered at a temperature of 100° F. by means of a soft rectal tube, inserted about six or eight inches into the rectum. Attached to the rectal tube by some two feet of rubber tubing should be a ten-ounce glass funnel into which the warm saline is poured, and which, after the flow into the bowel has been started, is adjusted to such a height as will allow of the flow to occur at the slowest possible rate; from ten to fifteen ounces should be administered at each operation, and to enable the flow to pass well into the bowel the patient's hips should be raised. The administration should be repeated every four, five or six hours, according to amount retained, endeavouring to get at least sixty ounces absorbed in the twenty-four hours.

As a rule the stomach, being at rest, contracts, and bleeding ceases spontaneously, the patient is comfortable and restful. This administration of saline should be continued for from forty-eight to seventy-two hours according to the severity of the hæmorrhage, when water in teaspoonful quantities may be tentatively administered by the mouth and increased as soon as it appears certain that it is well borne. During this period the mouth must be kept scrupulously clean and moist by the careful use of a suitable wash to obviate infection of the parotid glands through the ducts and consequent parotitis; as a further prophylactic measure, it is often advisable to induce slight salivary secretion by allowing the patient to chew a rubber teat or a piece of unflavoured chewing gum. A possible complication which must be watched for is the incidence of acid intoxication; the urine should be frequently examined for diacetic acid by the ferric chloride reaction and its appearance at once met by the addition of pure glucose (commercial glucose may contain arsenic in large quantities) in the normal saline in the proportion of from 3 to 5 per cent. Occasionally the patient is restless and alarmed, for which an initial dose of a quarter of a grain of morphia may be given subcutaneously or thirty grains of sodium bromide added to the first three or four salines. If in spite of this procedure the hæmorrhage recurs, then some styptic must be administered by the mouth; oil of turpentine I have found to be invariably successful; a tablespoonful is beaten into a fine emulsion with the white of an egg, and of this a teaspoonful is given every hour. The method sounds empirical, but it is one of the most certain, and the remedies are always to hand in practically every household. A method of administering turpentine which is not to be recommended consists in making the remedy more palatable by admixture with lemon-juice and sugar, since citric acid from its decoagulating action on the blood should be rigidly avoided. Of other styptics that may be employed, adrenalin chloride solution (1 in 1000) in doses of 10 to 20 min. in a tablespoonful of water may be repeated at intervals of three or four hours, or Liquor Ferri Perchloridi 30 min. in half an ounce of glycerine. Normal horse-serum also seems to exert a local styptic effect, and may be given in doses of 2 dr. in an ounce of water to be repeated in an hour if necessary.

If after a recurring hæmorrhage the rectal

salines are partly returned with decomposing blood, or if there is any marked intestinal distension from retention of such blood, the colon should again be washed out by a large soap-and-hot-water enema.

Rarely some difficulty in the administration of saline occurs from irritability of the rectum; this can generally be overcome by diminishing the amount at each operation and by the addition of 10 to 15 min. of Tinct. Opii to every second or third saline. Should it happen that absorption cannot take place sufficiently rapidly to meet or prevent urgent collapse, then an initial pint or two of normal saline should be given subcutaneously or intravenously.

During this period the patient receives nothing but saline solution, no attempt should be made to introduce food into the colon, the nutritive value of rectal feeding is very questionable, the nursing of the patient is unnecessarily complicated, the patient is rendered less comfortable, and is also exposed to toxæmia from absorption of products of putrefaction of the food introduced. Water alone is requisite and in sufficient quantity.

At the end of forty-eight or seventy-two hours half an ounce of sterilised water should be given by the mouth with a teaspoon, and if it produces no discomfort it should be repeated in half an hour, then freshly prepared albumin water is substituted, and two or three hours later milk diluted with an equal part of water, to which sodium citrate has been added in the proportion of two grains to the ounce. If at the end of six hours it is apparent that the half-hourly quantities of diluted milk are well borne, the amount may be rapidly increased, and at the same time the quantity of saline administered by the rectum correspondingly diminished. During the first twenty-four hours the patient should receive ten ounces of milk in which the whites of two eggs have been beaten up; it should be freshly prepared, kept on ice in a covered vessel and given hourly by means of a teaspoon; at the same time the patient may take gelatine jelly, allowing it to dissolve in the mouth.

On each succeeding day the amount of milk should be increased by two ounces, until the patient is taking thirty-six ounces in the twenty-four hours. On the second day the patient receives two whole eggs, and these are then increased one a day until the patient is taking six in the twenty-four hours; for the first five days the eggs are simply beaten up with the milk, on the sixth day one or two may be given in the form of custard. From the third day onwards the patient may also take an ounce of cream and an ounce of sugar, these being given partly along with the milk and egg and partly whipped into a foam with a little gelatine. On the seventh day the milk and eggs are given in part simply beaten up, in part as custard and in part as junket, also on this day the patient may be allowed a little sago, half an ounce boiled in milk, and a similar quantity of rusk grated in milk. On the eighth day the patient may be allowed an ounce of scraped raw meat divided into three doses, or two teaspoonfuls of somatose or plasmon. On the tenth day two ounces of tripe, raw or stewed in milk, or two ounces of scraped, lightly grilled steak, may be allowed. From the fourteenth day the patient is fed every four hours during the day, the diet being increased and varied by the addition of boiled calves' brains, minced boiled chicken, steamed plaice, thin split toast or rusk soaked in milk, and purée of potato and spinach in small quantity. Where whole milk gives rise to any discomfort, it may be modified by the addition of citrate of soda—two grains to the ounce—or by being treated with "Pegnin," a preparation which precipitates the casein in very fine curd; this so-called Pegnin-milk is pleasant to take, and is usually well tolerated when raw milk gives discomfort. The milk may also be diluted with lime-water or "Citoda," a citrated effervescent water. Or, lastly, it may be given in part as "malted milk."

Of drugs it is rarely necessary to administer any directed towards the gastric disorder; the bowels, which are ignored for the first four or five days, should then be maintained open by the daily administration of sufficient Carlsbad salt in eight ounces of hot water each morning.

From the fourteenth day onwards any anæmia should be dealt with by the soft mass of Blaud's pill in capsules, ten grains three times a day after food. When the patient experiences discomfort after food which cannot be overcome by varying the diet, some simple sedative as a mixture of bismuth carbonate and sodium bicarbonate with spirits of chloroform and peppermint water, may be given after food.

This method of dealing with ulcer from which recent manifest bleeding has occurred is one which experience has shown to be most efficient, but on the other hand certain authorities, led by Lenhartz, advocate a diet of which that begun in the schema on the third or fourth day is a modification, immediately following the hæmorrhage, and they report equally good results. It is well, however, to err on the side of conservatism in dealing with gastric hæmorrhage, and providing the patient receives a sufficient quantity of water, the starvation which absolute rest of the stomach entails is more than counterbalanced by the greater certainty of initial healing.

3. *Ulcers without Manifest Hæmorrhage.*—Rest and diet are the essential features of the treatment, drugs are subsidiary, and cannot be in any way regarded as a substitute. The patient should be confined to bed for at least four weeks in a recent ulcer, and for eight to ten weeks in ulcers of long standing. The mouth and teeth should be put into a thoroughly good hygienic condition. The colon should be evacuated by a soap-and-water enema. In cases of chronic ulcer where there is stagnation, the stomach should be carefully washed out with a soft velvet-eyed tube, twice or three times a week, using warm saline solution to which a drachm of sodium bicarbonate to the pint has been added, or warm Vichy water. It is also advisable to give the patient two or three test-breakfasts on consecutive mornings, consisting of ten ounces of weak tea without milk or sugar and four breakfast biscuits, the stomach contents being removed after the lapse of one hour, when by noting the amount of the contents withdrawn and the acid-values, free hydrochloric acid and total acidity, useful information can be obtained as to the secretory and motor activity of the stomach, which will provide a rational basis for the proper administration of neutralising and inhibitory remedies. It has been my experience that the nearer the ulcer is to the pylorus the greater is the acidity of the stomach contents and the greater the tendency to stagnation from pyloric spasm.

Moist heat should be continuously applied to the epigastrium for the first four weeks, either by simple fomentations, light poultices or a thermophor laid over a layer of moist flannel, care being taken that the skin does not become blistered or eroded. Such application, which is undoubtedly very soothing, appears to aid the healing process by inducing congestion, and at the same time serves a very important purpose in staying local spasm.

The diet must be so arranged that the patient receives the maximum nourishment with least bulk and in an unirritating and easily digestible form. Milk, cream, eggs, sugar, gelatine, constitute its basis, the quantities should be arranged according to the following schema—

	Day.						
	I.	II.	III.	IV.	V.	VI.	VII.
Milk .	10 oz.	15 oz.	20 oz.	25 oz.	30 oz.	35 oz.	40 oz.
Eggs .	2	3	4	5	6	7	8
Cream	½ oz.	½ oz.	1 oz.	1 oz.	1½ oz.	1½ oz.	2 oz.
Sugar	—	—	1 oz.	1 oz.	1 oz.	1 oz.	1½ oz.

At first the constituents are simply beaten up together, from the third day they may be administered in part as custard, junket and whipped and sweetened cream. The milk may be prepared with pegnin, or diluted with fresh barley-water, lime-water, or it may be citrated. For the first three days the patient is fed with a small spoon every hour, then to the end of the week every hour and a half. During the second week every two hours, the third week every three hours, and during the fourth every four hours. In the second week the patient also receives somatose, plasmon, sanatogen, valkasa, or other similar food proteins, and four eggs per day, one or two of which may be lightly poached, sago milk, split toast or rusk soaked in milk, stewed tripe, minced chicken or pigeon.

During the third week scraped underdone beef, thin stale bread in small quantity, butter. During the fourth week a small cup of weak tea, a little purée of potato, and various carbohydrate foods, as Benger's, Mellin's, Allenbury's, may be added to the daily dietary.

The bowels should be carefully regulated in recent ulcers after the third day, in chronic ulcers from the outset by the administration of some alkaline saline water, as ten ounces of warm Carlsbad water each morning on the fasting stomach.

Should the patient complain of thirst, it is better to give ten or twenty ounces of saline by the bowel than increase the amount of fluid by the mouth.

Medicinal Treatment.—Drugs are subsidiary to efficiently conducted rest and diet treatment, and in some cases may be entirely dispensed with. Where, however, there is considerable hyperacidity with associated discomfort or a tendency to spasm some time after food, alkalies, bismuth salts and belladonna by their antacid properties, are of great utility. A mixture of bismuth carbonate, magnesia, tincture of belladonna, or of bismuth carbonate and sodium bicarbonate, or sodium citrate and magnesia and tincture of belladonna, may be given ten minutes after food four times a day.

Various methods of drug treatment have from time to time been employed with the object of accelerating the healing process in the ulcer. Of these, treatment by bismuth salts is still practised, and in some cases with apparent success. In the usual practice of administering bismuth salts in an alkaline mixture after food, it is probable that the drug acts almost wholly as a neutralising agent; and in order that it may exert any protective or sedative action on the ulcer and thereby promote its healing, it is necessary that it be given in large doses and in the empty stomach. Fleiner, who systematised this method, advises the administration each morning after the fasting stomach has been washed out, of 150 to 300 gr. of bismuth subnitrate in 8 oz. of warm water by the stomach-tube, which is retained

in situ for that purpose; the tube is then partially withdrawn and the patient remains quietly in such position as it is believed will bring the drug in contact with the ulcer for five to ten minutes, the tube is then again pushed into the stomach and the excess of fluid withdrawn, and the tube removed. The patient continues in the same position for half an hour, when the first feeding is allowed. The method may be applied less rigorously by simply allowing the patient to drink the eight ounces of water in which the bismuth salt is suspended. In place of the subnitrate, bismuth carbonate, or a mixture of chalk and talc, or of bismuth carbonate and magnesia may be similarly employed, the subnitrate has the disadvantage of being an acid salt, whilst the carbonates may give rise to some distension by evolution of carbon dioxide. Further in place of simple water the salts may be suspended in warm Carlsbad water. It is not essential that the patient should assume any particular posture, as the drug is gradually disseminated over the whole mucosa and tends to collect in any depression that may be present, accordingly it is sufficient for the patient to lie quietly for half an hour before taking any food by the mouth.

Silver nitrate was formerly recommended as a remedy in gastric ulcer, one drachm of a 1 in 600 solution being given three times a day on the empty stomach, and gradually increased to one drachm of a 1 in 300 solution. In pill form it should not be employed. In several cases I have tried the effect of washing out the stomach every other morning with a 1 in 2000 solution for five minutes, finally running off the whole of the solution and washing out with normal saline; the results were certainly an improvement on those previously obtained in these cases by the bismuth method, and the method is worthy of further trial in suitable cases of chronic ulcer.

More recently normal horse-serum has been advocated as an antilytic in gastric and duodenal ulcers; the serum must be fresh, and is administered by the mouth immediately after food in doses of two drachms in half an ounce of water three or four times a day. I have, however, not been able to determine any particular benefit from its employment.

Of individual symptoms, pain and vomiting may by their predominance call for special treatment. The pain in gastric ulcer is in the majority of cases due to localised muscular spasm, occasionally to peritoneal irritation; morphia is contra-indicated in such cases owing to its stimulating action on gastric secretion, whereby the local condition is made worse while only the receptive centres are dulled; on the other hand, alkalies and belladonna with the local application of heat are efficient. In cases with persistent vomiting, should this manifestation fail to subside with variation of the feeding and the administration of bismuth salts in combination with bromides and belladonna, cocaine in doses of quarter of a grain in a teaspoonful of water ten minutes before food should be tried, and if this fails rectal salines employed exclusively for twenty-four or more hours.

Indications for Surgical Treatment.—Briefly, whenever the functional activity of the stomach is mechanically interfered with as by stenosis of the pylorus or body of the stomach (hourglass) or by perigastric adhesions; when in chronic ulcer the symptoms recur after a thorough rest-cure, and are of a nature that even for bare tolerance the individual is compelled to lead such a restricted mode of life as interferes with his temporal and mental welfare; when the life of the individual appears to be threatened by recurring hæmorrhage, and when there is any reason to suspect the possibility of the supervention of malignant disease, then surgical methods of treatment are indicated.

Cancer of the Stomach.—The medical treatment of cancer of the stomach is wholly palliative. The diet should be composed of fluid and soft foods, stimulating and nutritious, and any predilections of the patient should be met as far as possible. Beef-tea, meat extracts, with the addition of milk or eggs, coffee and milk, tea and milk, rusks, split toast, or crust soaked in milk, stewed tripe, minced chicken, scraped meat, lightly cooked eggs, custard, junket, and such carbohydrate foods as Benger's, Mellin's, Allenbury's, etc.

Of drugs, dilute hydrochloric acid in doses of 20 to 30 min., along with strychnine and infusion of condurango, should be given after food to assist the defective gastric activity. In some cases, however, it will be found that acids increase the discomfort produced by food, and in such a bismuth and soda or bismuth and magnesia mixture containing tincture of belladonna and tincture of Nux Vomica is more efficient.

Stenoses of the Stomach.—Permanent stenosis of the pylorus or of the body of the stomach (hour-glass stomach) is at once an indication for operative treatment, and only when this is not available is medical treatment called for. The indications are to maintain the motor activity of the stomach, to prevent any superadded spasm, to provide a diet which shall leave the stomach rapidly, to prevent stagnation, and, as but little water is directly absorbed from the stomach itself, to provide for this requirement of the individual in greater or less part by rectal salines.

Where the secretory activity of the stomach is normal or excessive as in cicatricial stenosis, the diet should consist of easily digestible proteins, of fats and a minimum quantity of partially dextrinised starchy food. Milk, cream, butter, custard, junket, underdone meat, steamed white fish, pigeon and chicken cooked in casseroles, rusks, split toast, bread crust, etc. Where, as in malignant disease, the secretion is defective, it is advisable to withhold fats—cream and butter—and to give stimulating foods as beef-tea, meat-juice, meat jellies, meat extracts, and such peptonised foods as milk, gruel, custard, Benger's food, malt rusks. The stomach should be washed out with an alkaline saline solution containing a drachm each of sodium bicarbonate and sodium chloride to the pint of warm water, or warm Vichy water every morning or every other morning according to the degree of stagnation and hypersecretion.

Of drugs, where the secretion is excessive, alkalies and belladonna after food are indicated, and where there is evidence of super-added spasm the meals should be preceded by a tablespoonful of olive oil or oil of sweet almonds; but where the secretion is deficient, dilute hydrochloric acid and strychnine also after food.

The treatment of the hypertrophic pyloric stenosis of infants should be conducted on the lines above indicated, the diet, however, being arranged to suit the age of the child.

Gastroptosis.—It is very probable that simple downward displacement of the stomach does not in itself give rise to any subjective manifestations of gastric disability, and that only with the supervention of atony in the body, (deficient peristole) does it become associated with subjective symptoms. Accordingly the treatment is that already described under *Atonic Dyspepsia*—that is, systematic abdominal massage, dieting and later some form of mechanical abdominal support, such as a simple well-fitting belt to support the lower abdomen, or a firm oval pad across the hypogastrium held in position by steel springs from dorsal pads much like the springs of a truss (Curtis), or the pneumatic belt of Charnaux. Support may be arranged by broad strips of strapping; this has the advantage that it can be applied to give support where and how it is needed, that it is more fixed; on the other hand, it is apt to be irritating and requires frequent renewal.

Nervous Disorders of the Stomach.—It would be perhaps more correct to describe the disorders included under this heading as nervous disorders with gastric manifestations. Aerophagia, or air-swallowing, rumination or merycism, and nervous vomiting. The treatment in all cases has to be directed to the general condition and to the nervous instability, primarily and chiefly, careful supervision, correction of bad habits (sexual perversion is not infrequently an important factor), moral suasion, isolation, a rigid course of Weir-Mitchell treatment, and of drugs, bromides in combination with large doses of valerian and of asafœtida. F. C. M.

TREATMENT OF DISEASES OF THE INTESTINES

DUODENAL ULCER

The treatment of duodenal ulcer does not differ from that of gastric ulcer (*q.v.*). But the tendency for a healed ulcer to break open again and for new ulcers to develop is greater, and consequently the after-treatment requires special consideration. It is not difficult to cause a duodenal ulcer to heal by suitable treatment in bed, but the unknown essential cause which led to the ulceration remains, and is probably still present for many years.

Special precautions are therefore required to prevent a recurrence, and it is generally advisable to give written instructions, which the patient should follow for some years or even permanently.

The teeth should of course be put into thoroughly good condition at the beginning of treatment, but the patient should in addition be instructed to have them overhauled at least twice a year, so that the slightest tendency to pyorrhœa alveolaris can be kept in check. He should eat slowly and masticate thoroughly; it is a good plan to give him solid food during the last fortnight of his treatment in bed instead of minced and pounded food, so that he may get into the habit of eating slowly, for when the habit is once acquired, it is easy to continue in the same way. It should be impressed upon busy men that it is better to eat nothing at all than to bolt unchewed food. When there is no time to sit down to a proper meal a glass of milk should be drunk or some chocolate slowly eaten.

Barclay and the author have shown with the X-rays that the stomach in patients with duodenal ulcer empties itself with excessive rapidity, in contrast with what occurs in gastric ulcer, when the evacuation is at the normal rate or delayed. The secretion of gastric juice continues, however, after the stomach is empty; it is the irritation of the duodenal mucous membrane by the undiluted and uncombined acid which causes new ulcers to form and scars of old ulcers to break down. The patient should therefore drink a glass of milk or eat a biscuit about two and a half hours after break-

fast and last thing at night in addition to taking his breakfast, lunch, tea and dinner, the time of which should be so arranged that not more than three hours elapse without taking food. The patient should have some food at his bedside to take at once if he wakes during the night.

He should avoid the pips and skins of both raw and cooked fruit, and pickles, salads and all cooked vegetables, such as celery, which cannot be chewed to a semi-fluid consistence; green vegetables are best given as purées with butter. No aerated drinks and no alcohol should be allowed, except a little very diluted whisky with meals for those who feel the need of it. Vinegar and acid fruit should be avoided, and salt fish and meat, high game, curry and made-up dishes should be prohibited.

Individuals with the duodenal ulcer diathesis frequently suffer from cold extremities, and attacks often begin within a few hours of exposure to cold. It is therefore most important to warn patients to keep their hands and feet warm; they should have a hot foot-bath before going to bed, and use bed-socks or a hot-water bottle if the feet are cold at night. They should change their clothes at once if wet through, and if they feel chilled they should have a hot bath and go to bed without delay. When possible they should live in a warm and equable climate and avoid the English winter.

The bowels should be kept regular, and this can be done most conveniently by means of oxide of magnesia, which should be given after each meal and with the intermediate feeds, as it then helps to neutralise the excessive acidity of the gastric contents. The most convenient way to take it is in a fluid preparation containing 5 gr. of magnesia to the drachm, from ½ dr. to ½ oz. being required as a dose.

If the patient is thin, he should take a tablespoonful of olive oil before each meal, as it is not only a very useful food but it diminishes the secretion of gastric juice. Liquid paraffin has neither of these actions, but if the magnesia does not suit or is insufficient to control the constipation, a tablespoonful may be given after one or more meals.

In severe cases it is advisable for a time to give 5 min. of tincture of belladonna half an hour before meals to reduce the acidity; this should be given again for a few weeks if there is a temporary return of symptoms, however slight.

Patients should be warned of the danger of recurrence, and should be told to go to bed on a milk-and-egg diet at the first suspicion of a return of symptoms. If they do this, treatment for twenty-four hours is often sufficient to ward off an attack. If, on the other hand, they wait until the symptoms become fully developed, a prolonged stay in bed will be required.

An operation should be advised under the following conditions—

1. At the earliest moment after a perforation.
2. For pyloric obstruction, even if this is so slight that it is only recognisable with the X-rays, no obstructive symptoms being yet present.
3. In the very rare cases in which the ordinary treatment with rest, diet and drugs does not relieve the symptoms.
4. When the symptoms recur after one or more courses of thorough medical treatment; the number of such courses which may be tried depends upon such circumstances as the age, social position, occupation and place of residence of the patient; thus the older a patient, the better his social position, the less strenuous his occupation and the less important occasional absences from business, and the warmer and more equable the climate the less urgent is the necessity for operation.
5. When more than one severe hæmorrhage has occurred or when occult blood remains in the stools after a severe hæmorrhage in spite of treatment.
6. When there is evidence of chronic appendicitis, as recurrences are likely to occur unless the appendix is removed. Appendicectomy without gastroenterostomy is probably sufficient in such cases. A. F. H.

Surgical Treatment of Duodenal Ulcer

Both clinically and in the text-books the individuality of duodenal ulcers has been overshadowed by the greater frequency of the neighbouring gastric ulcers. Our knowledge has been progressing steadily for years, but the greatest advance, with reference to the subject under discussion, has been in our cognisance of the interrelation of the different parts of the alimentary tract. The information was first gained from skiagraphic examinations made in search of the factors which cause intestinal stasis. It has been learned that when the ileum contracts the unhealthy duodenum writhes. Further, we have begun to believe that the comparatively late onset of symptoms in the subjects of duodenal ulcer, *e. g.* pain two hours after food, is due to this duodenal writhing. Hence, when the presence of a duodenal ulcer is ascertained, the physician in charge must not rest satisfied, but look for factors producing stasis in the ileocæcal region. For unless these ileocæcal factors are removed, when present, treatment of the duodenal ulcer will not be satisfactory. The relationship between the duodenum and the cæcal end of the ileum is close, but not fully understood at present. But it suggests an obvious reason for the success of appendicectomy, in suitable cases,

for appendix dyspepsia. It certainly constitutes the very first principle of the successful treatment of a duodenal ulcer.

It is agreed that all perforations of a duodenal ulcer have a solely surgical treatment. But it is necessary to call in the aid of surgery in some instances when the ulcer has not perforated. These must be briefly referred to for us to understand the principles of the surgical treatment of duodenal ulcers.

Pain.—This may be so severe or disabling as to call for the performance of a gastro-enterostomy plus occlusion of the pylorus.

Hæmorrhage.—This may demand similar surgical measures. But hæmorrhage from the main trunks of the pancreatico-duodenal vessels will not be stopped by any measure short of ligature of that vessel. It might be likened to the suggestion of doing a gastro-enterostomy alone for a perforation.

A dilated stomach, tetany, hypersecretion in the stomach, and perhaps *cholecystitis* and *pancreatitis,* which suggest an infective condition of the duodenum, are non-perforative conditions of a duodenal ulcer which demand operation. As years bring more knowledge to us it is seen that the medical treatment of duodenal ulcers is more and more relegated to the period before a diagnosis is made. As soon as the diagnosis is certain, surgical treatment is required.

In such treatment an anterior or a posterior gastro-enterostomy seems equally effective, provided the pylorus is narrowed or occluded by disease, stitching, band or ligature.

The perforation of an ulcer may be acute or chronic, intra- or extra-peritoneal. The acute are almost always intraperitoneal and most amenable to treatment. For success to be attained it is necessary that the diagnosis should be made quickly. Every few hours after the perforation make a great difference to the mortality from the condition. Surgical intervention alone can snatch the patient from death. The surgical procedures consist of—

1. An incision between the umbilicus and the pubes, to exclude appendicitis, salpingitis, etc., and enable the surgeon to cleanse, and perhaps, drain the flanks, iliac fossæ and pelvis.
2. A second incision is made through the medial part of the right rectus, above the umbilicus.
3. The perforated ulcer is then found, sutured, excised or tamponnaded according to the circumstances of the case and the predilections of the surgeon.
4. The peritoneal cavity is cleansed, by "sponging," not lavage, which would disperse the infection, and either closed or drained. Personally I feel sure that to drain is safer than not to drain.

A primary gastro-enterostomy is rarely needed; one, later and secondary, may be, particularly if the ulcer has been excised or successfully sutured.

Chronic perforations form localised collections of pus which require incision and drainage. Too often they are followed by the formation of a duodenal fistula requiring gastro-enterostomy plus pyloric occlusion.

In extraperitoneal perforations pain is usually the most marked feature. Gas escapes through the ulcer into the subperitoneal tissue so that the omentum, for instance, may be so "blown-up" as to look like lung. These extraperitoneal ulcers, if acute, are difficult to find, and are very fatal.

A chronic extraperitoneal perforation demands usually a gastro-enterostomy with pyloric occlusion. E. M. C.

DIARRHŒA

Acute Diarrhœa

Acute diarrhœa is always due to abnormal irritation of the colon, generally owing to the consumption of decomposing food or to an intestinal infection which results in the abnormal decomposition in the bowel of sound food. The patient should be kept warm in bed until all symptoms have disappeared. If he is seen within twelve hours of the onset, he should be given from $\frac{1}{2}$ to 1 oz. of castor oil to clear the irritant material out of the small as well as the large intestine, unless the diarrhœa is so severe that it appears probable that this has already occurred. When the stomach has been irritated at the same time it may be necessary to wash it out. No food should be given for twenty-four hours or even longer in severe cases, but the patient may drink as much water as he likes. Arrowroot made with water to which sugar can be added should then be given, but nothing else until the diarrhœa has ceased. Milk, junket, bread and butter and milk puddings should then be given and a gradual return should be made to an ordinary diet, the speed with which this is done depending on the severity of the case. Carbohydrates should be added to the diet before proteins, and meat should be given last of all, but after a severe attack the patient should avoid raw vegetables in the form of salads or pickles and excess of fruit for some weeks, as otherwise a relapse is likely to occur.

The only drug which is of real use in acute diarrhœa is opium and its alkaloids. If the diarrhœa shows no signs of abating after twenty-four hours some preparation of opium, morphia or codeine, should be given, the dose being regulated according to the severity of the diarrhœa and the general condition of the patient.

Chronic Diarrhœa

The successful treatment of chronic diarrhœa depends upon the recognition of its cause. Most frequently it is a result of excessive stimulation of the intestinal movements, but in some cases it is a result of over-excitability of the neuro-muscular mechanism which controls the movements. Those cases which are secondary to organic disease of the intestine, such as colitis and cancer, are separately considered.

1. *Excessive Stimulation of the Intestinal Movements.*—The treatment of this form of diarrhœa consists primarily in the removal of the cause. The question of diet first requires investigation. In some cases excess of vegetable food has been consumed, and a diet containing no vegetables, except potatoes, and no fruit, whether raw, cooked or as jam, will result in the disappearance of the diarrhœa. More commonly the diarrhœa is due to excessive fermentation of carbohydrates or excessive putrefaction of proteins. The character of the stool and especially the smell and reaction of a specimen after incubation for twenty-four hours indicate whether either of these conditions is present, excess of gas being produced in both cases; it is odourless in fermentative diarrhœa, but ammoniacal in putrefactive diarrhœa, the reaction of the stool being acid in the former and alkaline in the latter instead of almost neutral. In *fermentative diarrhœa* starch should at first be completely excluded from the diet, but sugar, malt extract and milk are allowed. When the diarrhœa has stopped, cellulose-free starch, such as arrowroot, may be given, but no potatoes, white bread or rice for several weeks, and no vegetables containing a greater quantity of cellulose until still later.

A lacto-vegetarian diet is most suitable for *putrefactive diarrhœa.* Some of the milk may be replaced by sour milk. No meat should be allowed until the diarrhœa has ceased for a fortnight.

A rare but important form of chronic diarrhœa is that which occurs in achylia gastrica, the absence of gastric juice allowing the passage of an abnormal quantity of organisms and of undigested meat into the intestines, with the result that excessive putrefaction is likely to occur. This *gastrogenous diarrhœa* rapidly improves on the diet already described as suitable for putrefactive diarrhœa, but a relapse is certain to follow a return to an ordinary diet unless hydrochloric acid is given. The patient should take at least 15 min. of the dilute acid during and again after each meal for the rest of his life, unless the achylia is due to chronic gastritis, in which case the normal secretion of gastric juice may eventually return. The acid may be added to the water the patient drinks during his meals; if a little albumen and sugar are added it is not unpleasant and most patients eventually become accustomed to it.

The chronic diarrhœa which sometimes occurs in Graves's disease, uræmia and septicæmia disappears as the primary condition improves. As symptomatic treatment, the subcutaneous injection of 2 min. of adrenalin chloride three or four times a day is often very efficacious in the diarrhœa of *Graves's disease,* whilst that of *uræmia* may cease on reducing the quantity of protein in the diet.

2. *Nervous Diarrhœa.*—Under normal conditions the entry of food into the empty stomach gives rise to a gastrocolic reflex, which is the chief stimulus to the movements of the colon. In most individuals this is only followed by defæcation after breakfast, as the pelvic colon is then full and the sudden passage of fæces from it into the rectum gives rise to the call to defæcation. In individuals with an abnormally excitable nervous system the gastrocolic reflex may cause a further quantity of fæces to reach the rectum after each meal. Such individuals generally pass a formed stool immediately after breakfast; this is often followed by one or more loose stools, additional ones being also passed after lunch and dinner, especially if the patient is particularly anxious that his bowels should not open, but is frightened that they will do so. Such cases are hardly influenced by diet, but drugs which diminish the activity of the gastrocolic reflex, either peripherally or centrally, are very effective. A mixture containing 5 gr. potassium bromide and 5 min. tincture of belladonna taken half an hour before meals is generally all that is required in mild cases; in severer cases a small dose of codeine should be added. The exact dose of each drug requires modifying to suit each patient, as different individuals react very differently to these drugs, especially to belladonna. Arsenic has been recommended for these cases, but I have rarely found it of much use, and in some cases it has actually aggravated the condition. When the diarrhœa has been completely controlled the dose of the drugs should be gradually reduced and their use can finally often be discontinued, at first before lunch and dinner and finally before breakfast, without any return of symptoms. In most cases it is still advisable to allow the patient to have the medicine or a pill containing belladonna and codeine always with him, so that he can take a dose before going to a dinner party or on any other occasion when he fears that he will have diarrhœa. He soon learns to trust so thoroughly in his pill that it probably acts more by suggestion than in any other way, and the dose can accordingly be progressively reduced until it is infinitesimal.

In many cases of diarrhœa due to other causes the bowels act most frequently after meals. In such cases the treatment just described is often of use in conjunction with that required for the primary condition.

A. F. H.

CONSTIPATION

For the rational treatment of constipation it is necessary to distinguish between the three great classes of cases: (1) that in which the passage through the colon is delayed, whilst defæcation is normal—colonic constipation; (2) that in which there is no delay in the arrival of fæces in the pelvic colon, but their final excretion is not adequately performed—pelvirectal constipation or dyschezia; and (3) that in which the quantity of fæces found is insufficient to produce an adequate stimulus to the intestinal movements and to defæcation.

Hygiene of the Bowels.—In no circumstances should the patient fail to make an effort to open his bowels after breakfast, even if he feels no desire to do so, and a call to defæcation felt at any other hour in the day should be obeyed at once at whatever inconvenient time it may occur. Sufficient time should always be spent over the act of defæcation, and it may be advisable to pay two visits to the closet at short intervals. In order to prevent the temptation to hurry over defæcation the closet should be clean, devoid of smell and properly warmed in winter. In dyschezia a footstool nine inches lower than the seat should be provided, so that the crouching position may be assumed during defæcation.

Diet.—It is important to see that sufficient food is taken, as constipation is often as much due to its insufficient quantity as to its unsuitable quality. The diet should contain an increased proportion of fat and of vegetable foods, especially those which contain much cellulose, organic acids and sugar. Thus green vegetables or salads should be taken twice a day, and fruit, whether fresh or dried, raw or cooked, at breakfast, lunch and dinner. In addition to that taken with meals, a glass of cold water should be drunk before breakfast, another just before retiring to bed and perhaps a third half an hour before dinner.

Drugs.—The majority of cases of constipation can be cured without drugs, if proper treatment is instituted at a sufficiently early stage. In dyschezia purgatives are either absolutely useless, or they only have an effect when fluid stools are produced, a considerable quantity of fluid and nutritive material being thereby wasted. In curable diseases, such as chlorosis and neurasthenia, and in incurable diseases, such as Bright's disease, diabetes and insanity, all of which are aggravated by constipation, purgatives should be regularly given. They are also useful for making the stools soft when defæcation is painful as a result of inflamed hæmorrhoids or anal ulcer and in diseases of the pelvic organs, and when straining at stool is accompanied by danger, as in patients with cardiac degeneration and in those liable to cerebral hæmorrhage on account of high blood pressure. In cases of constipation due to other causes, in which non-medical treatment proves insufficient, purgatives must also be used, but an effort should be made to dispense with drugs at the earliest possible moment. The stool produced by an aperient should be normal in size and consistence, and should not deprive the body of any water or nutritive material which ought to be absorbed. The dose should be so regulated that one stool is passed every day and the desire to defæcate is felt immediately after breakfast. The aperient should cause no pain or discomfort, and should not irritate the intestinal mucous membrane sufficiently to produce any inflammatory change. If it is probable that the purgative will be required permanently, one such as aloes, cascara or senna should be chosen, which is likely to maintain its good effect without any increase in the dose being required.

In constipation due to a greedy colon the bulk of the fæces must be increased by the administration of some unirritating substance, such as liquid paraffin or agar-agar, which passes through the intestines without undergoing decomposition or absorption. Liquid paraffin is particularly valuable when the fæces are hard and dry; it is therefore useful in other forms of constipation besides that due to a greedy colon, as, for example, in diabetes. In dyschezia also the soft stools which result from its use are expelled with less difficulty than ordinary fæces. From 1 dr. to ½ oz. should be taken with meals two or three times a day.

Enemata.—The majority of cases of moderately severe constipation are more or less cumulative, excess of fæces being always present in the large intestines. It is therefore necessary that the colon should be completely evacuated before other methods of treatment are adopted. It is generally possible to empty the bowels completely by means of a dose of castor oil, followed, if necessary, by a saline purge. In severe cases, however, it is necessary to remove the accumulation of fæces from the large intestine by enemata before other treatment is attempted, and in rare instances the rectum can only be emptied by means of the finger.

It is essential in treating dyschezia to keep the rectum and pelvic colon empty so that they may in time regain their normal tone and contractile power. This can only be accomplished by the regular use of enemata of water

or glycerine. The bulk of the water enemata and the strength of the glycerine enemata should be gradually reduced. As a rule the tone and contractile power slowly return and a cure finally results.

Hydrotherapy.—A cold bath or a cold douche after a hot bath is a very valuable addition to the series of stimuli which lead to the morning evacuation. The spasm in spastic constipation is often benefited by a hot bath, and when constipation is due to some painful pelvic condition, the latter and the associated spasm of the sphincter ani may be relieved by the use of a hot sitz-bath.

Rest, Exercise and Massage.—In neurasthenic constipation, and whenever the patient is under-nourished, rest in bed for some weeks is very beneficial, and if sufficient food is taken, the bowels may act without the aid of drugs or enemata. Regular exercise in the open air is one of the most important means of preventing constipation, especially in individuals who follow a sedentary occupation. It increases the appetite, diverts the mind, strengthens the voluntary muscles of defæcation and stimulates the intestinal movements. When any of the voluntary muscles of defæcation are weak, considerable benefit can be gained by the performance of Swedish exercises every morning and evening. Whenever constipation is due to want of activity of the intestinal musculature, the condition of the latter may be improved by deep abdominal massage, the efficiency of which is greatly increased if the masseuse gives the first treatment under the X-ray screen after a barium meal so that she can see exactly what manipulations are required to act upon the colon, and to restore a dropped colon to the normal position.

Dyschezia is often associated with visceroptosis, both being due to weakness of the abdominal muscles. In such cases a proper support is of great value.

Spa Treatment.—Many patients, who are unwilling to undergo any systematic treatment for constipation at home, readily agree to devote a few weeks in the year to a "cure" in some popular health resort. The removal from business and household worries, daily exercise in the open air, regular hours and the change from rich food to a suitable diet are of much more importance than the drinking of waters, which could be done equally well at home, if they were really needed. In most of the resorts which are regarded as suitable for constipated patients, excellent arrangements are at hand for hydrotherapy, massage and electrical treatment, and better results are obtained from intestinal lavage in such places as Harrogate, Llandrindod Wells, Plombières and Châtel-Guyon than at home.

Operative Treatment.—When constipation is the result of definite organic obstruction of the intestine, surgical treatment is clearly indicated. Unfortunately several operations have been recommended in the last ten years for the relief of constipation in the absence of this clear indication, and consequently the results hitherto obtained have only been satisfactory in a comparatively small proportion of cases. Surgical treatment should not be recommended for chronic constipation unless all of the following conditions are fulfilled :—

1. Prolonged medical treatment has failed to give relief. By "relief" I do not mean cure, as many patients continue to be completely relieved of their constipation and the symptoms to which it has given rise so long as they continue medical treatment.

2. An accurate diagnosis is essential. The part of the bowel in which stasis is present must be accurately determined as well as the presence or absence of dilatation, narrowing or adhesions; in the case of the latter an attempt must be made to ascertain how far, if at all, they interfere with the normal intestinal functions. An X-ray examination of the stomach and intestines should therefore always be carried out, and the rectum and pelvic colon should be examined with the sigmoidoscope as well as with the finger. The history should be taken with great care and the patient's other organs thoroughly examined in order to determine whether the intestinal condition is primary and the cause of all the symptoms.

3. The operation should be chosen to suit the particular condition found. It is clearly absurd to recommend appendicostomy, ileo-sigmoidostomy or colectomy as the routine treatment for a condition which has such a manifold pathology as constipation. In some of the rare cases in which surgery is required, one or other of these operations may be indicated, but in others an operation devised to short-circuit or excise the affected part only and not the whole colon should be performed.

4. The dangers and possible unpleasant sequels of the operation should be weighed against the severity of the symptoms, for which it is proposed to operate. Appendicostomy is almost free from danger to life, but in rare instances unpleasant local complications have occurred. All the other operations, which have been recommended for constipation, have a definite danger. The mortality of simple short-circuiting operations is small, but it is greatly increased if adhesions are divided at the same time, and the mortality of partial and, to a still greater extent, that of complete colectomy is high, even in the most skilful hands. It is clear, therefore, that such operations should not be lightly recommended, and that they should only be performed for symptoms which are really

severe enough to interfere considerably with the enjoyment of life or with the performance of the professional or other duties of the patient.

A. F. H.

SURGICAL PRINCIPLES IN THE TREATMENT OF APPENDICITIS

At the outset it should be made clear that the present article is not concerned with the treatment of acute perforative or "septic" appendicitis with early symptoms of general peritonitis. I have elsewhere endeavoured to point out that where there is the slightest doubt in such cases, early and immediate operation is imperative. In this article we are concerned only with what I may term (1) *Acute Appendicitis* in its early stages, (2) *Chronic Appendicitis.*

Under *acute appendicitis* I class those cases where, in addition to the localising symptoms of appendicitis—pain, tenderness, vomiting—there is evidence of septic absorption as shown by fever, increased pulse rate, leucocytosis.

Under *chronic appendicitis* those cases are considered in which there is evidence of septic absorption, and where the symptoms of appendicitis may be doubtful, and perhaps only localised after prolonged and careful examination has excluded other conditions; or even those cases where the only "evidences" of appendicitis may be symptoms of colitis, dyspepsia, or even chronic constipation. These chronic cases show a variety of macroscopic conditions of the appendix, kinking, thickening of one part, stenosis of the proximal part, adhesions, etc.; microscopically, varying degrees of destruction of the mucous membrane, round-cell infiltration of the submucous and muscular coats, concretions and contents of various degrees of septicity are found.

In *acute appendicitis* the treatment should be unhesitating; in all such cases I believe that immediate removal should be insisted on. Should the patient refuse when the position has been fairly and carefully explained, the responsibility is no longer the doctor's, and the usual palliative measures should be adopted—absolute rest in bed, fluid diet, ice-bags to the abdomen, small doses of belladonna, and above all a careful watch on the pulse-rate and temperature. Small enemata may be given to clear the lower part of the large intestine, but no active purgative should be given by the mouth.

In advocating immediate surgical operation on all cases of appendicitis which come under the class I have taken as *acute*, I am well aware that I may be addressing myself to some readers who will continue to regard it as merely the promptings of a surgical mind, "Oh," they will still continue to say, "many cases get perfectly well by careful dieting without operation." It may be so, yet I cannot help wondering whether such cases were ever really *acute* appendicitis. To attempt to convert such minds is perfectly idle; like that voracious bird the ostrich—who, by the way, has not got an appendix—they deliberately push their heads into the sand and shut their eyes to the tragedies that are *always* around us; a fatal case of appendicitis is to them as inevitable (and as infrequent) as is the death of an "air-man." Such opinions are now fortunately those of only a small and decreasing minority; the vast majority of practitioners, physicians, and surgeons are *now* in agreement.

The reasons for this opinion are shortly these—

1. The patient's safety; for the risks of an early operation are very small indeed, while it is well known that the symptoms from hour to hour cannot be relied on—pulse rate, pain, muscular rigidity, all may be deceptive. It is impossible to diagnose the absence of pus, and in many a patient for some time after actual perforation appears to be better.
2. If pus *has* formed the sooner it is drained the better. Moreover, the chance of removing the appendix before an abscess cavity has formed is much greater, while drainage in a doubtful case relieves pain and distension, and can do no harm.
3. If pus is not present, despite our diagnosis, the patient is taking no risk and will recover more rapidly than if he is left to face unnecessary risks and submit after convalescence to an operation "à froid." My own experience is that although there is often considerable difficulty in these early operations there is no increased risk to the patient. The essentials of success are: (1) patience and great gentleness on the part of the surgeon; (2) haulage and stimulation of the intestines after the methods of the sausage-maker are not to be recommended; (3) use iodine catgut throughout; (4) a long external incision; (5) muscle splitting and carrying the incision between the muscle fibres if necessary down the posterior wall of the sheath of the rectus (to get more room I would advocate an incision in the linea semilunaris, despite other opinions, in all cases where pus is believed to be present); (6 protection of the whole abdominal wall after the peritoneum has been opened by rubber tissue. After the operation the patient is kept sitting up, and castor-oil is given within thirty-six hours of the operation, and the treatment continued if necessary as in that for ileus of septic peritonitis.

Treatment of Chronic Appendicitis.—Here the practitioner should be assured that if the case *is* really one of chronic appendicitis it is most improbable that any measures short of removal

of the appendix can be of avail. It will be conceded that acute appendicitis is probably the result of a flare-up of chronic appendicitis, and, most usually therefore, if we are sure of our diagnosis, the patient's safest course is to have the appendix removed at a time when there is practically no risk at all in the operation. Moreover, as my old friend Mr. C. B. Lockwood has often insisted, even when we see the appendix we cannot judge of it by its exterior; an apparently normal appendix is often like the "goodly apple," and it is becoming more and more evident that chronic appendicitis is often responsible, either for intestinal stasis and its ill effects, for gastric or duodenal trouble, or, on the other side, for setting up most obstinate colitis, and that removal of the appendix will cure none of these conditions when once they are established.

I have been profoundly astonished at the rapidity with which extensive changes occur in the appendix by the following. I operated some years ago on a woman for a most troublesome left pyosalpinx. At the time of the operation the right tube and ovary were normal. I looked for and carefully examined the appendix, which was (externally) perfectly normal. The operation had been a long one, and I did not think I was justified by adding to its length. Just three and a half months after the operation the patient came back complaining of attacks of abdominal pain and constipation (there were no localising symptoms). I opened her abdomen again, believing I would find pelvic adhesions. There were no adhesions, but the appendix was now about four and a half inches long, dilated to the size of the little finger, with two large concretions in it at its tip, completely filling it. Mindful of this case, and being convinced of the entire absence of additional risk, I am personally in the habit of removing the appendix in all abdominal cases where the patient's condition is satisfactory, and I can get at it. (I do not suggest, of course, making an incision unnecessarily long, or making a second incision for this purpose.)

On the other hand, we must not fall into the error of considering every case of abdominal pain to be due to inflammation of the "nuciform sac" beloved by playwrights, and even cases of pain and tenderness in the right iliac region are not necessarily due to appendicitis. Many such cases need most careful and prolonged watching; the possibility of renal or ureteral calculi, gall-stones, calcareous mesenteric glands, early spinal caries, psoas abscess, sacro-iliac disease, and right ovarian or tubal disease have all to be considered, and the aid of the physician and radiographer is indispensable.

In all such cases every possible attempt should be made to diagnose the cause, and the patient's pulse and temperature should be observed for a considerable time. If we can exclude conditions other than those which require operation, then I believe an operation should be undertaken, and this may frequently be of an exploratory character. I have assisted a surgical colleague in operating on a lady whose only symptoms were pain and tenderness referred to the appendix region. At the first operation a diseased appendix was found, *also* an unruptured tubal gestation sac. After some months exactly similar attacks of pain occurred, and a considerable number of minute gall-stones were found to be the cause. The motto "Wait and see" is held by some to be an excellent one, but in chronic appendicitis, as in acute, the waiting may be too prolonged, and visual inspection may either (1) disclose more than is anticipated, or (2) be conducted in the post-mortem room.

J. K. M.

COLITIS

(*a*) Non-Ulcerative Colitis

1. **Acute Colitis.**—The treatment of acute non-ulcerative colitis is the same as that of acute diarrhœa (p. 299), as it is produced by the same causes, the presence or absence of actual colitis depending upon the severity and the duration of the irritation of the mucous membrane. When colitis is produced, the after-treatment requires to be much more prolonged than in simple acute diarrhœa; it does not differ from the treatment of chronic infective colitis.

2. **Chronic Infective Colitis.**—An attempt should be made to ascertain the source and the nature of the infection. Pyorrhœa alveolaris and other septic conditions of the mouth, nose and pharynx require treatment, and the possibility of contamination of the water supply and of milk or other food should be investigated; if there is any doubt, all water and milk should be boiled and no raw vegetables or fruit should be consumed.

Sour milk exerts a marked inhibitory influence on the development of intestinal organisms; it is consequently very useful in some cases of infective colitis, especially when the stools are offensive and alkaline. It is important that a pure and active culture of the Bulgarian lactic acid bacillus should be used in its preparation. All the solid, and many of the fluid, commercial products are either completely inactive or very impure, containing a large proportion of streptococci, with few or no lactic acid bacilli. Very little should be given at first in order to ascertain how the individual reacts to the treatment.

My experience of autogenous vaccines in infective colitis is not favourable, as I have seen the condition greatly aggravated by their use,

large mucous casts instead of small quantities of uncoagulated mucus being passed after the first injection.

In the majority of cases excessive putrefaction takes place in the colon. It is then advisable to give a diet containing a minimal quantity of animal proteins for some time. In this way putrefaction is greatly reduced and the absorption of toxins is so much diminished that symptoms of auto-intoxication gradually disappear. In some cases only a few days of this treatment are necessary, but in severe cases it may be advisable to continue it for as long as three months. At first no animal food should be given at all, milk and eggs being prohibited as well as meat. In severe cases it is advisable to begin with foods such as sweetened arrowroot and water, which contains little or no cellulose. During this period constipation may occur, and the bowels have to be opened by means of paraffin and, if this is insufficient, by the use of enemata; it is important, therefore, to increase the quantity of ordinary vegetable food as soon as possible. After some improvement has occurred in severe cases, and from the beginning of treatment in milder cases, milk can be given; after a short period eggs, and subsequently fish, chicken and meat can be added to the diet. If enemata are required a solution of some such antiseptic as sodium salicylate (30 gr. to 1 pint) should be used.

3. **Chronic Catarrhal Colitis.**—Chronic catarrhal colitis is most commonly due to the irritation of the intestinal mucous membrane by hard fæces. It is often aggravated by the injudicious use of aperients and excess of vegetable food leaving a coarse residue. Hence, when constipation is complicated by catarrhal colitis, liquid paraffin should be used instead of vegetable aperients, and the less coarse vegetable foods, and those which depend on their chemical rather than their mechanical properties, should be given. In chronic cases treatment by intestinal lavage at one of the health resorts mentioned in the article on constipation should be advised.

4. **Muco-membranous Colitis.**—Patients suffering from muco-membranous colitis should be treated with the object of removing the two underlying factors—the abnormal condition of the nervous system and the constipation. It is most important to discourage the patient from making minute investigations of his stools; he should be told to be satisfied if he feels better without looking to see how much mucus is passed.

In severe cases it is advisable to begin the treatment with an unstimulating diet, such as milk, to which arrowroot and other cellulose-free carbohydrates can be added. As soon as some improvement has occurred, and in milder cases from the onset of symptoms a generous mixed diet should be given. Thin and anæmic patients, who have often unwisely restricted their diet, should be encouraged to eat, as they are unlikely to recover until they have gained weight. The diet should contain a plentiful supply of those articles, which are useful in uncomplicated constipation, on account of their chemically stimulating properties, but salads, pickles, fibrous vegetables, the skins and pips of fruit, whether raw, cooked or in jam, and the coarse varieties of whole-meal bread and oatmeal, should be avoided; in severer cases green vegetables should be passed through a sieve and given as purées. Mustard, pepper and spices of all kinds should be prohibited. It is desirable, especially when intestinal sand is passed, to replace as far as possible the saturated fats, such as stearin and palmitin, which form a large percentage of the fat in meat, butter, cheese and cream, by unsaturated fats, such as olive oil. It is most important that the food should be thoroughly masticated.

At the beginning of treatment every trace of fæces accumulated in the colon must be removed. This can best be done by the combined use of castor oil and enemata. Once the colon is empty, the re-accumulation of fæces can often be prevented by the administration of liquid paraffin or agar-agar in order to soften the stools. If a satisfactory stool is not passed each day, the further treatment depends upon whether the X-rays have shown that the stasis is in the proximal part of the colon, in which case aperients are required, or in the pelvic colon, when treatment by enemata without aperients is indicated. In most cases the best aperient is castor oil, half an ounce or an ounce taken last thing at night or on waking in the morning being generally required, but in some patients senna pods or saline aperients act better.

As in the case of uncomplicated spastic constipation, belladonna is the most useful drug for combating the intestinal spasm, but in many cases small doses of bromide should also be given in order to diminish the irritable condition of the nervous system. When the pain is severe it may be necessary to add codeine to the belladonna; the patient should be kept in bed and warm applications made to the abdomen.

Local treatment of the mucous membrane of the colon by means of enemata should only be used when other treatment has failed to give relief. As the patients are always self-centred they should not be encouraged to concentrate upon their bowels by irrigating the colon unless this is absolutely necessary. I have, indeed, seen improvement result from discontinuing intestinal lavage, which had been continued for too long a period, almost as frequently as from a course of the same treatment given to

patients who had not previously tried it. Intestinal lavage can be given at home, but it is generally more effective when carried out at Plombières, Châtel-Guyon, Harrogate, Llandrindod Wells, Bath or Buxton. Normal saline solution should be used if the treatment is given at home, and injections of soap and water, antiseptics and astringents should be avoided, as they tend to aggravate the condition by irritating the mucous membrane. At the various spas the natural waters are generally used for the purpose. The effect of the intestinal douches is much increased if the bowels are previously opened, either naturally or with the aid of a mild aperient, or an enema of olive oil or paraffin, given the evening before and retained during the night.

Various operations have been performed for intractable cases of muco-membranous colitis. When any condition, such as appendicitis, which is amenable to surgical treatment, appears to be the cause of the muco-membranous colitis, this should, of course, be dealt with. In the very exceptional cases, in which all other treatment fails to relieve the associated constipation, especially if the latter is due to stasis in the proximal as well as the distal colon, an appendicostomy should be performed, so that the colon can be washed out through the opening with two or three pints of warm normal saline solution every morning if possible, after the bowels have acted naturally. The irrigations should not be discontinued until at least three months have elapsed since the disappearance of all symptoms. The result of the operation is, however, not always satisfactory, and with the closure of the opening there is a considerable tendency to recurrence, as the underlying nervous condition remains unaffected.

Ileo-sigmoidostomy and colectomy should only be performed in the very exceptional cases in which the indications given in the section on the treatment of constipation are fulfilled.

A. F. H.

(*b*) Ulcerative Colitis

(*vide* also *Dysentery*).

If a sigmoidoscopic examination is always made when a patient passes blood or mucus in his stools or is suffering from diarrhœa, the cause of which is not obvious, ulcerative colitis can often be recognised at such an early stage that it is still amenable to medical treatment. Such treatment must always be prolonged, and no case can be regarded as cured until a further sigmoidoscopic examination has shown that all ulceration has disappeared. Symptoms frequently disappear weeks or even months before healing is complete, especially if the patient is kept in bed; this is the cause of the very frequent relapse after an apparent cure, but if all the ulcers have really healed there is no great tendency to recurrence.

The patient should be kept in bed until no blood has been passed for four weeks and the bowels are opened not more than twice a day. The rest of the treatment should be continued until no ulceration can be seen with the sigmoidoscope, but the diet should not be altered until three months later, and if the stools tend to become hard they should be kept soft with liquid paraffin for six months.

A generous diet should be given, and if, as is often the case, the patient has lost weight, two or three pints of milk should be given in addition. All food which could irritate the colon mechanically should be prohibited; vegetables are only allowed if they have been passed through a fine sieve, and no fruit except in the form of jellies should be given. Tough meat, porridge and whole-meal brown bread are prohibited. The indications for sour milk are the same as in simple infective colitis, and, as in that condition, pyorrhœa alveolaris or other sources of sepsis in the mouth, nose, or pharynx should be removed. All food must be thoroughly masticated.

In all cases the colon should be irrigated with astringent solutions every day. The bowels should previously have been opened naturally; if in the later stages of treatment there is a tendency to constipation, sufficient liquid paraffin should be given to make this possible, but should the bowels even then be insufficiently emptied, a plain water enema must be given before the irrigation. A pint and a half of fluid should be run in very slowly at a pressure of not more than eighteen inches of water; the tube should only be inserted just beyond the anal canal, as otherwise it curls round the rectum and rubs the ulcers, which generally extend to the beginning of the anal canal. I have found with the X-rays that fluid injected in this way invariably reaches the cæcum, so that the whole of the ulcerated mucous membrane is treated, as the ileum is never affected. The fluid should be retained for gradually longer periods up to half an hour.

I have generally used silver nitrate solution for the irrigations, beginning with a strength of ½ gr. to 1 oz., and gradually increasing to 2 gr. to 1 oz. Recent investigations show, however, that albargin (1 gr. to 1 oz.) would probably be more efficient; it has the further advantage that the subsequent administration of an enema of normal saline solution in order to prevent the absorption of the soluble silver salt is unnecessary.

It is always advisable to examine the stools bacteriologically, and to test the opsonic index of the blood against the different organisms found. In my experience, however, vaccine treatment has generally very little effect, but

if the active organism is identified with certainty, vaccination may be tried in addition, though never as a substitute to other treatment.

Intestinal antiseptics have very little, if any, effect; if sour milk is given they would probably diminish or totally prevent its activity. When the diarrhœa is particularly severe opium may be required.

When for any reason a patient is not willing to undergo prolonged medical treatment, which necessitates at least four weeks in bed and sometimes very much more, when medical treatment does not produce rapid improvement, and, when the case is already chronic or unusually severe when it first comes under treatment, an appendicostomy should be advised. The indications with regard to diet and vaccine treatment are the same as if no operation had been done, and the bowel should be irrigated twice a day with the same fluids as are used for irrigations from the rectum. In the later stages liquid paraffin should be given to prevent the formation of hard stools, and the opening should not be allowed to close until two or three months after a sigmoidoscopic examination has shown that all ulceration has disappeared. A. F. H.

SURGICAL TREATMENT OF DISEASES OF THE COLON

The greatest difficulty in the treatment of diseases of the large bowel is often the making of an accurate diagnosis as to the cause of the trouble. The colon is a very inaccessible portion of the human body, and when the site of the disease is unknown it is not easy to diagnose the condition correctly, or to ascertain the position and nature of the lesion. There are, however, several means at our disposal by which we can obtain accurate and reliable data to aid us in diagnosing the cause of the symptoms and the situation of the lesion. Thus we have the sigmoidoscope, X-ray photographs taken after a bismuth meal or after the injection of bismuth solutions into the bowel, examination under an anæsthetic, and chemical and bacteriological examination of the stools. It is usually necessary to employ several or all of these in the same case, and carefully to compare the results, and examine them in reference to the symptoms and history before attempting to make a diagnosis. In any difficult case it is seldom either possible or feasible to attempt a diagnosis as to the condition present in the colon from a single examination. Most of the failures in treatment of diseases of the colon are due to the want of a correct diagnosis rather than to any mistakes or lack of knowledge in the treatment itself. The diagnosis is, therefore, a matter of primary importance.

Treatment of Congenital Abnormalities of the Colon.—Congenital abnormalities of the colon are comparatively rare and but few of them are amenable to treatment. The commonest forms of abnormality of the colon are those in which there is some failure in the descent of the cæcum; in other words, where there is some congenital abnormality of the mesenteric attachment. One of the most important of these is the condition in which the cæcum and ascending colon have a common mesentery, and any condition may be found between this and the whole of the cæcum and ascending colon being attached by the same mesentery as the small intestine. When there is a long common mesentery to the cæcal angle there is always a possibility of its becoming twisted and producing a volvulus. This condition is generally described as volvulus of the cæcal angle. Usually the twist occurs around the ileum as an axis. The twist may occur in either direction, but the commonest direction seems to be that from left to right. A volvulus of this description is an exceedingly serious lesion, as it may involve nearly three quarters of the entire intestine. Dilatation occurs rapidly, and the symptoms are very obscure, though it is obvious that some obstruction exists. The only treatment consists in opening the abdomen and discovering and untwisting the volvulus. This should be done through a large incision in order to get a clear view of the parts, as the condition found is usually exceedingly complicated.

Congenital Dilatation of the Colon.—The non-operative treatment of this condition consists in careful regulation of the bowels by means of aperients and enemata. Abdominal massage and the application of the galvanic current have also been advocated. Unfortunately, these are merely palliative measures and only act by preventing the onset of acute obstruction, which is liable to occur at any time. The only chance of curing patients with this condition lies in operation. It is, however, very important that the patient should not be operated upon during an attack of acute obstruction. Colotomy, which is generally a fairly safe operation, is exceedingly fatal in these cases. Out of fourteen cases treated by colotomy which have been collected by the author, no less than eleven died. This is accounted for by the fact that the colon owing to its immense size cannot be drawn out of the wound, and all that it is possible to do is to establish a fæcal fistula into the dilated portion. Owing to the great weight and thick muscular walls of the bowel in these cases, there is a grave risk that the stitches will be torn away and that the patient will die from acute peritonitis. Colotomy should, therefore, be either entirely avoided in treating cases

of acute obstruction, or the colotomy should be done above the affected bowel.

The best results in these cases have followed resection of the dilated portion of the colon. This is obviously an exceedingly difficult and serious operation. The bowel in some of these cases may measure as much as nine inches in diameter and be an eighth of an inch thick. A considerable portion of the large bowel may be involved; great difficulty is therefore likely to be experienced in its removal, and it is not an operation to be lightly undertaken. Excellent results, however, have followed resection of the colon in these cases. In all but two of a number of collected cases in which this operation was performed the dilatation was confined to the pelvic colon. In one case, however, the entire colon was successfully resected for this condition. It must be noted that in three instances the dilatation of the colon has recurred after resection, and that a second resection has become necessary.

In one case the author performed appendicostomy for dilatation of the colon, the operation being done in the hope of preventing accumulation in the enormously distended sigmoid by washing out the colon daily. The patient, a man aged twenty-two, was quite well between the attacks of obstruction from which he suffered, and it did not seem justifiable to subject him to excision of the enormous loop of distended bowel unless every other method had failed. The results of this operation were very satisfactory, and no further attacks of obstruction had occurred up to two and a half years after the operation, at which time the patient was lost sight of.

Chronic Obstruction of the Colon due to Adhesions.—These cases form a very important group, as this condition is not infrequently accountable for the severe auto-intoxication which is occasionally met with, and to which considerable attention has lately been given. When a patient recovers from general peritonitis extensive adhesions between the different parts of the bowel are undoubtedly left; but there is abundant evidence to show that these may in course of time entirely disappear. Occasionally, however, for reasons which we do not quite understand, the adhesions remain and cause serious trouble. Where there are extensive general adhesions little is to be hoped for from operative treatment. Curiously enough, however, there is, as a rule, no serious trouble where the adhesions are extensive, and it is in the cases where there are a few localised adhesions that the most trouble results. The commonest situation for these localised adhesions is the sigmoid colon, and less commonly, the right flexure and cæcal angles. There is still considerable doubt as to whether these adhesions are congenital or acquired, though the writer is of the opinion that they are usually of an acquired character.

The diagnosis of such adhesions is often a matter of great difficulty, but the sigmoidoscope and examination by X-rays will usually render the diagnosis almost certain. Bands of adhesions causing kinking of the pelvic colon must be very carefully sought for, as they may be easily overlooked even when an exploratory laparotomy is performed. As a rule, little is to be expected from non-operative treatment in these cases beyond amelioration of symptoms, and usually before they reach the surgeon all the ordinary medical measures have been tried. Operative treatment consists in separating or dividing the adhesions and re-establishing the normal course of the bowel. It is further necessary, in order to prevent a recurrence of the condition, carefully to restore the peritoneal surface, so that no uncovered area is left which may be the starting-point of fresh adhesions. Many of the failures in the past have been due to insufficient attention being paid to this point. Most careful asepsis and hæmostasis are absolutely essential to secure a successful result in these cases. Where it is not possible satisfactorily to divide the adhesions, or where there would be risk in so doing, a short circuit of the obstructing angle, or resection of the involved portion of the bowel will generally be found to be the best treatment. The actual details of the operation naturally vary in every case.

Chronic Mucous or Membranous Colitis.—It is usually only in the worst cases of this condition that the aid of surgery is sought. But it frequently happens that purely medical treatment fails to give relief, and then, as a last resort the surgeon is called in. The opinion of the writer has always been that in the majority of cases in which the patient passes mucus in large quantities associated with abdominal pain and discomfort, there is no colitis in the direct sense; that is to say, the bowel is not inflamed. In these days by means of examination with the sigmoidoscope it is usually possible to distinguish those cases due to definite inflammatory lesion, and in these latter cases alone are satisfactory results to be hoped for from medical treatment. In the cases in which no colitis is found, the cause of the symptoms must be sought for in some other lesion in the abdominal cavity; and in the writer's experience such a lesion is nearly always present, though it may be difficult to find. Among such causes may be mentioned a chronically inflamed appendix, cancer, disease of the uterus or appendages, movable kidney, visceroptosis, gallstones, and aneurysm of the aorta. The obvious treatment, and the only

one likely to be successful is to find the cause of the symptoms and to remove it. This will often necessitate an exploratory laparotomy, as the diagnosis must frequently be in serious doubt. Such cases of colitis are always secondary and should not really be included under this heading, although, as already mentioned, they form a large percentage of the cases seen.

Apart from these cases surgery has attempted to deal with chronic colitis by two methods—(1) by establishing an artificial anus on the right side so as to give rest to the colon, and (2) by performing an appendicostomy which enables the large bowel to be kept constantly washed out. The first method, while sometimes successful, has now been completely discarded in favour of the second, which gives quite as good results and without any of the serious discomforts attached to a right-sided colotomy. Although it must be admitted that in many of the cases in which appendicostomy is performed a complete cure does not result, yet very great improvement is the rule, and in many instances it is possible to close the opening at the end of a few months. As appendicostomy does not cause the patient any inconvenience and the operation is not attended with any serious risk, it is well worth trying when other methods have failed, and should certainly be preferred to the establishment of an artificial anus.

Left inguinal colotomy has also been performed, but is quite unsound, as if the lesion is confined to the rectum it can be satisfactorily dealt with by local injections or ionisation, without having recourse to a colotomy; while if the disease involves the whole colon, no good results can be expected from a colotomy on the right side.

Ulcerative Colitis. — Up till comparatively recently cases of ulcerative colitis had been given no special treatment, or had been treated only by restricted and special dietary combined with attempts to wash out the lower bowel with antiseptic or silver solutions. It was found, however, that treatment on these lines was exceedingly unsatisfactory. A very large proportion of the patients died, the death-rate from ulcerative colitis at several of the large London hospitals being found to be nearly 50 per cent.; and, moreover, recurrences were very common, even when recovery occurred under such treatment. Out of sixty cases collected by the writer in 1910, thirty-three were treated medically and twenty-seven by operation. The mortality in the non-operated cases was 78 per cent., while in the operated cases it was only 22. It must also be remembered that at that time cases were only operated upon when they were practically *in extremis*, whereas now that the value of early operation is becoming recognised the mortality has been still further reduced. There is only one satisfactory way of treating cases of ulcerative colitis, and that is by immediate operation. The writer is of opinion that provided the cases are not left till too late recovery is almost certain with operative treatment. The best method is to perform an appendicostomy, and in the severe cases to follow this up with washing out the bowel every three or four hours with warm water; in the less severe cases irrigation twice a day will usually be found sufficient. It is to be remembered that many of these patients are very ill and are not able to stand a severe operation. Fortunately, appendicostomy is one which can be carried out quickly and without any serious disturbance of the patient. The results are very satisfactory. Bleeding and diarrhœa are generally controlled within forty-eight hours of the operation, and after this healing of the ulcerated areas occurs rapidly. At first it is wiser to use only plain warm water for the irrigation; in the later stages, where an astringent appears to be advisable, 0·5 per cent. argyrol or protargol may be used. On no account, however, should antiseptic solutions be pumped into the colon, as a serious amount of absorption is liable to occur. The irrigation of the bowel through the appendicostomy opening should be continued until the ulceration has quite healed and all symptoms have disappeared. After that it is not advisable to let the opening close for a full year, as relapses are by no means uncommon; they may, however, be easily dealt with as long as the opening is patent. At the end of a year, if there has been no relapse, the patient may usually be considered cured, and the opening can then be allowed to close up.

The formation of an artificial anus on the right side has also been tried in cases of ulcerative colitis; but it appears to have no advantages over appendicostomy, while it has several very obvious disadvantages. But in any case, whichever operation is performed, everything depends for success upon the operation being done early. In severe cases of ulcerative colitis patients go downhill very rapidly, and operation is not given a fair chance if it is performed when the patient is already in an exhausted condition with an extensively ulcerated colon, although even then excellent results are sometimes obtained.

Pericolitis.—This curious condition has only been called attention to within the last few years. In the typical condition there is a tight stricture, usually in the pelvic colon, often of a tubular character, and causing considerable tumour formation so that a swelling is often felt in the left iliac fossa. The condition is easily mistaken for malignant disease in the

sigmoid colon. In most cases the condition arises from diverticulitis of the colon, there being numerous little pouches or herniæ of the bowel containing fæcal concretions, around which chronic inflammation has occurred with the deposit of large masses of dense fibrous tissue. The stricture is, as a rule, densely adherent to the neighbouring parts. This condition is a simple inflammatory one and not malignant, although it closely resembles the latter condition. Chronic obstruction is the typical symptom which calls for treatment. In some cases, however, formation of an abscess or perforation of the bowel from the giving way of one of the diverticulæ is the first sign of trouble. The only treatment which can be of any use is operation. The ideal treatment is to resect the diseased portion of bowel and to sew up the ends so as to restore the continuity of the colon. This operation has now been performed successfully in a considerable number of cases, and the patients have completely recovered. In some cases, however, it is not possible, either on account of adhesions, the situation or the size of the stricture. The case may then be treated by short-circuiting the stricture or by the performance of an ileo-sigmoidostomy. As an alternative to this we may perform a colotomy above the strictured area, and where the patient is very ill or there seems reason to suppose that a short-circuiting operation is unduly risky, the formation of a temporary colotomy is the best treatment, and the question of removing the stricture may subsequently be discussed.

Tuberculosis of the Colon.—This condition is met with in three forms: (1) As part of a general or miliary tuberculosis. (2) Secondary tuberculous ulceration. (3) Hyperplastic tuberculosis. The last is the only condition in which tubercle occurs as a primary lesion in the colon. In the other two forms it is, as a rule, secondary to tubercle of the lungs; but in the third it certainly appears to be primary in the large bowel. As regards symptoms in diagnosis, hyperplastic tuberculosis of the colon closely resembles pericolitis due to diverticulæ. There is usually a large tumour and a tight stricture of the bowel, with great hypertrophy of the bowel wall. Except as a secondary complication ulceration is unusual. A very rare form is that called "gas-pipe colon," in which almost the whole length of the colon is involved, and is converted into a stiff strictured tube with thick walls, often mistaken for carcinomatous colon.

The treatment for this condition is the same as for pericolitis, namely, resection where possible, and short-circuiting, or exclusion with colotomy where a resection is not feasible.

The Treatment of Severe Cases of Chronic Constipation.—It is difficult to bring the treatment of this condition within the scope of a short article. The cases brought to the surgeon are those in which almost every form of medical treatment has been tried, and in which it is yet impossible, or almost impossible, to get the bowels to act with any regularity. The first essential in such cases is to ascertain the mechanical cause of the condition, if one is present. This is often a matter of considerable difficulty, but much help can be obtained by a sigmoidoscope examination, X-ray examinations, and careful examination of the patient. Where a mechanical cause can be found, such, for instance, as a chronic volvulus, adhesions, stricture, etc., the proper treatment is a laparotomy for the correction of the obstruction by suitable means. In those cases where there is no definite obstruction, and where the condition is due to a general atony of the bowel, the only treatment, if all medical measures fail, is appendicostomy, or in a few cases, ileo-sigmoidostomy.

Embolism of the Mesocolic Vessels.—This is a very rare condition, and one which is seldom diagnosed except on a postmortem table. The symptoms are those of acute obstruction in a patient in whom an embolus is probable. When the condition is diagnosed during life the only treatment which has led to success is resection of all that portion of bowel involved by the embolism.

Treatment of Tumours of the Colon

Simple Tumours.—Isolated polypi or adenomata of the colon are sometimes by means of the sigmoidoscope. They vary in size from quite small pedunculated growths to masses as large as a strawberry. They give rise, as a rule, to bleeding, and occasionally to intussusception. If left alone they tend to become malignant. The proper treatment wherever such a condition is diagnosed is the free removal of the polypus, together, if possible, with some portion of the bowel wall. There is a rare condition in which there are multiple polypi throughout the colon. Many hundreds, or even thousands, of polypi may be found scattered throughout the large intestine, and in such cases the patients suffer from very severe diarrhœa and bleeding. The condition is usually diagnosed by means of the sigmoidoscope, but the treatment is a matter of the greatest difficulty. There is a very marked tendency for one or more of the polypi to become malignant in course of time. The only treatment which would appear to have any serious chance of success is excision of the entire large intestine.

Malignant Tumours.—Cancer of the colon tends to remain localised and does not readily

give rise to secondary gland involvements or to metastatic deposits. The results of resection in such cases are often very satisfactory, and as quite large portions of the colon can be removed without seriously affecting the patient's subsequent health, malignant growths in this situation are particularly suitable for operative interference.

We must recognise the difference between treatment of a case of obstruction of the colon due to cancer, and the treatment of a case of cancer of the colon without obstruction. In the former condition the operation is performed for the relief of the obstruction, and in view of the very serious condition of the patient's health from the obstruction, an elaborate operation for the removal of the growth is not possible. All that can be done, as a rule, is to open the bowel above the growth; or, in favourable cases, to bring that loop of bowel containing the growth out of the abdominal wound. In the latter case a subsequent operation for the removal of the growth will be necessary. When, on the other hand, there is no obstruction present, a carefully planned operation can be carried out with the object of widely excising the growth, together with the contiguous portion of mesocolon and any glands in the neighbourhood. The ends of the bowel may then be sutured together so as to restore the continuity of the lumen.

The operation may sometimes be done in two stages, that portion of bowel containing the growth being first of all short-circuited, and at a subsequent operation the involved loop removed. This operation is particularly suitable in cases of cancer at the cæcal angle, and can often be used in cases where the left or right flexures are involved. Short-circuiting is also a good operation in cases of inoperable cancer of the colon, as it considerably prolongs the patient's life by preventing the possibility of obstruction.

The technique of these various operations cannot be gone into in this article. We can only say that very careful operating is necessary in order to obtain good results in cases of anastomosis of the large intestine.

J. P. L. M.

THE TREATMENT OF INTESTINAL OBSTRUCTION

The term "Intestinal Obstruction" includes three clinical conditions that differ widely in the pathological process giving rise to them and the clinical signs and symptoms produced. They call for accurate differentiation, since the success of the treatment employed depends largely upon the period at which it is undertaken. It is the custom to divide cases of this kind into three groups: viz. (1) Acute Intestinal Obstruction, (2) Chronic Intestinal Obstruction, and (3) Chronic Intestinal Obstruction becoming acute. This division, however, seems to imply that the difference between the groups is merely one of degree, and that the same causes are at work in all of them but with a varying intensity: this is not actually the case, and this fact should be kept in mind, since confusion of thought may lead to confusion in practice, which, in these conditions, may be attended with serious results.

It is difficult to suggest names for these three groups of cases that are not open to objection on the score of precision, but perhaps the following may help to keep before the mind of the observer the more prominent of the factors at work. The nomenclature suggested is as follows—

1. *Intestinal Strangulation.*—This group corresponds closely to that commonly called Acute or Sudden Obstruction, except that it obviously should embrace those cases of external hernia that have become strangulated: to exclude these from the cases of intestinal obstruction and to relegate them to a mere division of hernia is, perhaps, the best way of causing the practitioner to make the serious and common mistake of not inquiring and examining for an external hernia as the first step in the examination of any suspected case of intestinal obstruction. It is also open to the objection that those cases of obstruction due to thrombosis of the superior mesenteric vessels which are strictly included in this group cannot be regarded as cases of strangulation, but for all practical purposes it is very useful, since in all the members of this group—and there are many—there is a much graver cause at work than mere interference with the passage of the intestinal contents: the blood-supply of a portion of the bowel is interfered with, and it is to this factor that the speedily fatal result is due if prompt and efficient treatment is not adopted.

2. *Complete Intestinal Stasis.*—This term is not above reproach, since complete intestinal stasis must also occur in all cases of intestinal strangulation, but for want of a better it is used in this connection to denote the cases that are essentially chronic in nature, in which only the circulation of the intestinal contents—as opposed to the intestinal blood-supply—is interfered with and in which the obstruction has reached such a degree that neither gaseous nor solid matter can pass. This group corresponds to that termed chronic intestinal obstruction becoming acute, and is to be preferred inasmuch as the older term seems to infer that the type of obstruction has changed, whereas really it is only the symptoms that become acute, not the type of obstruction.

3. *Chronic Intestinal Stenosis.*—In this great group of cases there is only one influence at work, namely a gradually increasing difficulty in the onward passage of the intestinal contents. Eventually the obstruction may become complete.

A consideration of the foregoing classification will make it clear that in the first group of cases the main factor is sudden and severe obstruction to the intestinal blood-supply, followed rapidly by death of the affected area of the bowel: in the second there is complete occlusion of the intestinal lumen, leading to rapid decomposition of the arrested intestinal contents with resulting general toxæmia and local intestinal irritation; and in the third group there are the results produced by the efforts of the bowel to overcome the gradually increasing difficulty in the propulsion of its contents. It will be well before describing the prominent signs of each group of cases, to go into the differential diagnosis between intestinal obstruction as a whole and the various other conditions that may occur in the condition known as the "acute abdomen"; after that the symptoms special to each variety of obstruction and the appropriate treatment will be considered.

The Differential Diagnosis between Intestinal Obstruction and Other Forms of Abdominal Mischief.—Since it is common for a certain amount of *intestinal stasis* to occur in most acute abdominal conditions, it is obvious that the mere cessation of the passage of fæces and flatus is not in itself sufficient to entitle one to make a definite diagnosis. In cases of complete stasis, however, the patient is generally keenly conscious of his inability to pass anything, and often says that if he could do so he would be all right. Some *pain* is also complained of in all cases of "acute abdomen," and hence this symptom is not often very helpful unless inquiry elicits the fact that it was paroxysmal at its onset and was unaccompanied by tenderness in the earliest stages of acute strangulation: indeed, sometimes pressure seems to relieve it. The *vomiting* is rarely typical—and it is important not to wait until it becomes feculent. There is always an absence of *pyrexia* in cases of primary obstruction, and in those beginning with elevation of temperature some other cause must be looked for. This is a most useful point in diagnosis. Any case of "acute abdomen" beginning without elevation of temperature must be either an intestinal strangulation, a colic (hepatic or renal), a hæmorrhage or a perforation. The uncontrollable agony and intense collapse serve to distinguish a colic, while the signs of a hæmorrhage soon become obvious and a perforation will generally be made manifest by the sudden collapse followed by a rise in temperature and pulse rate. *Abdominal tenderness and distension* are usually absent in the early stages of the acute cases, but occur later on as toxic symptoms develop. In cases of complete stasis, however, they are early signs. We may summarise the symptoms of intestinal obstruction thus: In acute intestinal strangulation there is sudden acute abdominal pain, generally of a griping character and often relieved by pressure, followed in a very short while by violent vomiting which rapidly becomes "feculent." At the same time there is the characteristic "abdominal expression" and complete inability to pass fæces or flatus—at any rate after the lower bowel has been emptied. There is no pyrexia, the pulse is not rapid, and there is no abdominal distension. Later on distension occurs and the temperature and pulse rate rise.

In complete intestinal stasis and chronic intestinal stenosis there is little difficulty in the diagnosis—except in those cases of the former group in which no history of previous obstruction can be obtained. Even in these, the onset of complete obstruction is very obvious to the patient; and when this occurs in connection with an absence of pyrexia, and is accompanied by a painless distension of the abdomen and vomiting, persisting on the ingestion of food until it becomes feculent, there can be little doubt as to the cause, though the whereabouts of the obstruction may be uncertain.

The different conditions producing obstruction give rise to different symptoms and may call for different kinds of treatment. It will be well, therefore, to describe each variety and its treatment separately.

Intestinal Strangulation (*Acute Intestinal Obstruction*) occurs most frequently in the small intestine, and its most common causes are strangulation of a hernia (external or internal), strangulation beneath a band, volvulus and intussusception: to these must be added the acute obstruction caused by thrombosis of the superior mesenteric vein. The chief feature in these cases is the extreme urgency of the symptoms and the severe depression of the patient. The onset is sudden and is marked by sharp pain of a griping or colicky nature, soon followed by persistent vomiting which rapidly becomes feculent; there is complete obstruction to the passage of fæces and flatus. The patient always looks pinched and anxious, and may be severely collapsed. The pulse and temperature at first are normal and there is no abdominal distension.

In the case of an *external hernia* there are the well-known local symptoms of strangulation in addition, viz. increase in size, dullness on percussion, tenderness on pressure and irreducibility of the hernia. In the case of an internal hernia the pain may be localised, and after a

short time there may be definite tenderness on pressure over the site of the hernia.

An *intussusception* presents certain special features that should enable it to be diagnosed as such before operation. There is intestinal tenesmus with the passage of blood-stained mucus unaccompanied by fæcal matter, and the characteristic sausage-shaped tumour caused by the intussusception may be felt extending obliquely across the abdomen from the right iliac fossa to the splenic flexure. This alternately contracts and relaxes, and thus varies in consistency though it never disappears completely.

In a *volvulus* there is very early distension of the twisted coils of gut. The acute form of this condition is rare.

Treatment of Intestinal Strangulation (*Acute Intestinal Obstruction*).—The treatment of all these cases is to relieve the constriction by surgical means at the earliest possible moment. Not an hour's unnecessary delay is permissible. The diagnosis must be made as soon as possible after the patient is seen, and the abdomen opened directly arrangements can be made for doing so. There should be no attempt to wait and see what will happen; if the practitioner is in doubt as to whether the case is one of strangulation or not, it will be safer to open the abdomen at once and see the condition of affairs rather than to wait a few hours and give the bowel an opportunity to become gangrenous, as it will often do in a very short time. It is quite impossible to form any opinion as to the severity of the strangulation, or, therefore, of the rapidity with which gangrene will occur. No drug treatment is of avail. When the diagnosis has been made and arrangements are in progress for operation—and not otherwise—morphine may be administered. But when once this has been done, the operation must be carried out, however much improvement the morphine may appear to make. Before operation the stomach should be washed out to prevent flooding of the air passages during anæsthesia. The incision—in default of any localising symptoms—should be paramedian and sub-umbilical, and the further treatment will vary with the condition found and the state of the strangulated bowel. In all cases of hernia, the neck of the sac is dilated or divided and the hernia reduced; bands are ligatured at each end and removed; volvuli are untwisted, and an intussusception is reduced by squeezing the intussusceptum very carefully out of the intussuscipiens. When the strangulation has been relieved by one or other of these methods, the condition of the coils of bowel affected is inspected. If the peritoneal coat is shiny and has not lost its polish anywhere it is safe to close the abdomen and expect recovery, but if the bowel wall has lost its polish, and especially if any part of it has become dull and sodden and of a dirty greyish-black, the part will inevitably die and further steps must be taken. Small areas may be inverted by Lembert's sutures, but large ones demand immediate resection of the affected area and either immediate re-union, or the establishment of a temporary artificial anus followed later by a reunion. The choice between these methods depends largely upon the condition of the patient and the probability of his being able to stand so serious an operation.

Complete Intestinal Stasis (*Chronic Intestinal Obstruction becoming Acute*) may be due to any cause producing chronic intestinal obstruction (see below) and occurs when the degree of obstruction is so great that the intestinal contents fail to pass. The complete blockage may be temporary—as when it is produced by the irritation of purgatives or food above a stricture—or permanent, as in many cases of volvulus, intussusception, or kinks. In these cases there is generally—though not always—a history of previous obstructive symptoms such as constipation alternating with diarrhœa, flatulence, indigestion, and gradual increase in size of the abdomen. The completion of the obstruction is marked by entire arrest of the intestinal contents, which is accompanied by steadily increasing distension, increasingly painful peristalsis, and finally vomiting, which becomes feculent if allowed to persist. There is no elevation of pulse or temperature until secondary changes in the bowel wall set in.

The diagnosis in these cases is quite easy. The patient is intensely conscious of the obstruction, and for a long time it is merely the obstructive symptoms that are in evidence. Later in the case stercoral toxæmia sets in and may then overshadow the obstructive symptoms.

Treatment.—When the obstruction is complete, as it is in all these cases, the most pressing indication is to relieve the stasis and thus check the intestinal decomposition which, by the production of various toxines, not only produces local lesions of a severe type, but also gives rise to general toxæmia from which the patients frequently die. The urgency of the operation is not quite so great as it is in cases of strangulation, since there is no question of imminent gangrene of the bowel, but intestinal decomposition is going on all the time—even though the vomiting may be checked by withholding food by the mouth—and toxæmia is becoming established. Therefore operation should be urged without delay, and the practice of withholding food by the mouth, feeding by the rectum, and waiting on the chance of the obstruction giving way should be sternly discouraged.

There are two ways of relieving the obstructions met with in these cases. One is to open

up or remove the obstruction and so allow the intestinal contents to pass *per vias naturales*; the other is to establish an artificial anus above the obstruction without relieving the latter. The former procedure is obviously to be preferred when it is possible to carry it out, but reflection will show that in many cases it is fraught with so much danger that it is more in the patient's interest to carry out some other procedure. When the obstruction has lasted a considerable time, and especially when the patient is fat and elderly, the toxæmia already present may be so severe that no extensive operation is likely to be tolerated and it becomes clear that the one indication that the surgeon has to bear in mind is to remove the fermenting contents of the bowel as rapidly as possible, and with as little shock to the patient as may be, and postpone to a more suitable occasion all idea of radical procedures. One may summarise the methods at the surgeon's disposal thus—

1. Simple laparotomy and establishment of a permanent artificial anus. This is the operation of choice in an irremovable and unrelievable obstruction, such as cancer of the rectum.

2. Laparotomy and the establishment of a temporary artificial anus. This is the treatment for all those cases where the obstruction is removable, but the patient's age or general condition precludes this being done at the time the operation for relief of the obstruction is undertaken.

3. Laparotomy, removal of the obstruction and establishment of a temporary artificial anus. This applies to cases where the obstruction can be removed but the patient's general condition is too bad to render it safe to restore the alimentary canal after this has been done; a second operation for the restoration of the bowel can be undertaken when the patient recovers from the first.

4. Laparotomy, removal of the obstruction, and re-establishment of the intestinal canal without forming an artificial anus. This method is suited for cases in which the obstruction is due to a foreign body inside the bowel, pressure upon it from tumours outside, volvuli, or some of the rarer cases of malignant or innocent stricture in which the patient is comparatively young, the toxæmia very slight, and the operation for removal of the obstruction and repair of the bowel easily and rapidly performed.

5. Laparotomy, removal of the obstruction and immediate re-establishment of the intestinal canal with the formation of a temporary fæcal fistula in order to drain the bowel above the original seat of obstruction and obviate all risk at the line of union from distension or absorption. This is the best method to employ when the patient's condition and the nature of the obstruction allow of it. The fæcal fistula is allowed to close spontaneously, or, if it fails to do so, a plastic operation is undertaken for its repair.

Pending operation in all these cases all food should be stopped by the mouth, only water and such drugs as salol, β-naphthol, or boric acid, which tend to promote fermentation, administered. Lavage of the stomach often relieves the distress considerably and should always be practised immediately before operation. Morphine is only to be given to allay pain and check unduly vigorous peristalsis when operation has been arranged for.

Chronic Intestinal Stenosis (*Chronic Intestinal Obstruction*).—In these cases the symptoms of gradually increasing obstruction are quite clear, and the only difficulty in the diagnosis is the nature and situation of the obstruction. Gradually increasing abdominal distension, flatulence, indigestion, constipation alternating with diarrhœa and colicky attacks call the attention of both patient and doctor to the condition, and then careful search will reveal the cause.

Treatment.—Obviously this lies in removing the cause, and equally obviously this should be done before the patient has had time to suffer from toxic absorption from the bowel or generalisation of the disease should this be of an infective or malignant nature. An early laparotomy should be undertaken after all information has been obtained by means of bismuth meals, sigmoidoscopic examination and palpation under an anæsthetic, and any lesion found dealt with by appropriate surgical means. Medical treatment should only be indulged in while an attempt is being made to establish a diagnosis. F. F. B.

THE TREATMENT OF PERITONITIS

Acute Peritonitis

Acute Peritonitis may be *general* or *localised* to a particular region.

Acute General Peritonitis

The moment the diagnosis is made the surgeon's aid should be called in with the least possible delay. In this serious condition the only chance that the patient has of recovering is immediate laparotomy, which will give the surgeon an opportunity to remove the cause or to identify the organism to treat, by drainage, the accompanying peritonitis. It is evident, therefore, that the rôle the physician will play in this condition is (1) in the preoperative stage; (2) in the post-operative stage.

1. In the Pre-operative Stage

Position.—The patient should be put to bed in the position which will give him most ease;

this will usually be found to be in the semi-recumbent (Fowler's) position. A pillow placed under the knees, by relaxing the abdominal muscles, will also assist him. If this position is assumed the infection is restricted, as far as possible, to the pelvis; and further, when the patient is aged, to prevent any complication and reduce any distress falling upon the heart through flatulent distension, this attitude is of great value. If the patient complains of the weight of the bed-clothes, a cradle should be used.

Diet.—All food by the mouth is withheld, not only because a general anæsthetic may be at any time required, but also because the peristalsis which the ingestion of food stimulates, will be exceedingly painful and the movements of the intestines will open up channels for the dissemination of any purulent matter.

Thirst and Restlessness.—In addition the patient may suffer from thirst and restlessness. Both these may be relieved by the administration of rectal injections consisting of 10 oz. of a saline solution, 1 dr. to the pint, which may be given every two or three hours. Instead of this solution a 5 per cent. solution of glucose is sometimes used.

Medicinal treatment is in this stage entirely symptomatic. The most prominent symptom is pain; the only drug that will certainly give relief is morphia. It is of the very first importance that the symptoms should be left unmasked by the temporary amelioration afforded by the administration of morphia, for the most misleading picture may subsequently be afforded. If possible morphia should be rigidly withheld until after consultation with the surgeon. Once it has been decided to perform an operation there is no objection, if the pain renders its administration imperative, to a small dose hypodermically, *e.g.* $\frac{1}{5}$ gr. with $\frac{1}{100}$ gr. of atropine sulphate. "Pain and anxiety do more harm than a small dose of opium."

Hot stupes or fomentations to the abdomen very often afford considerable relief. These applications should be as light as possible in weight, and most conveniently take the form of thin cloths wrung out in hot water.

A complete examination should be made with as little disturbance to the patient as possible, to ascertain the condition of his heart and lungs and any other organs which will indicate the suitability or otherwise of a general anæsthetic, and supply any other information which may be of service to the anæsthetist.

Shortly before the patient is put upon the table he should empty his bladder, and when vomiting is taking place the stomach should be washed out with warm water containing sodium bicarbonate, 20 gr. to the ounce. In urgent cases this can be performed and a catheter passed when the patient is under the anæsthetic.

The preparation of the skin is of course left to the surgeon.

2. Post-operative Treatment

Position.—After the operation the patient is quickly put back in a bed thoroughly warmed with hot-water bottles, care being taken to protect him from any risk of being burned by them. An electric blanket is sometimes used instead of a hot-water bottle.

Immediate treatment to a large extent depends upon the condition of the patient. If there is much shock or collapse he must lie flat and the foot of the bed should be raised upon blocks. As soon as possible, however, the patient's position should be altered and the semi-recumbent, or Fowler's position, resumed. Once the patient has been placed in a comfortable attitude it is extremely important to alter his position as little as possible. Any such movement may set up an attack of vomiting, and in certain cases disturb the heart's action. Should the necessity for moving him arise, plenty of assistance should be procured in order that he may be shifted with the minimum of disturbance. Whilst the patient should be left alone as far as possible, constant watching is essential. There is never the slightest reason, indication, or justification for awakening a patient from sleep, and, indeed, sleep is often prevented by too active attention in nursing, or the too frequent giving of medicines. All mental excitement must be strictly prevented and visitors must not be permitted for at least twenty-four hours after the operation.

For the *shock* hypodermic injections of strychnine or adrenalin may be necessary.

Saline infusions should be started immediately. The most convenient method is by the rectum, but urgency may necessitate the administration subcutaneously or intravenously. When the stage of collapse has passed, saline infusions will still be continued, since by their aid the toxins are diluted.

In short, the effective treatment (apart from that of symptoms) resolves itself into the administration of as much fluid as possible, and this is best achieved by saline infusions. Normal saline is generally used, but the hypertonic solution known as Ringer's fluid is preferable. It has already been noted that the form of administration depends upon the urgency, and, if possible, the slowest form of all—rectal injection—should be selected. A malleable tube bent so as to lie on the bed is inserted for two or three inches, to this the ordinary infusion apparatus is attached. The temperature of the solution when it reaches the rectum

should be 100° F., and it should be allowed to pass into the rectum not faster than one pint an hour. A feeling of distension or other discomfort usually denotes that the fluid is being injected too rapidly, and this will be immediately relieved by retardation or stoppage of the flow. As a rule 4 to 5 pints will be easily borne, and much larger quantities have often been administered. The success or failure of the proceeding depends upon constant attention. Pituitary extract is valuable in combating the shock since it raises the blood pressure. Details as to the method of administration are given below under "Flatulence."

Vomiting.—Post-anæsthetic vomiting will usually continue for the first twelve hours, although in some cases hardly any disturbance of this kind occurs. It will generally be relieved by a teaspoonful of sodium bicarbonate in half a pint of warm water, which washes out the mucus and the remains of the anæsthetic from the stomach. As a variant, which is often more convenient, sips of hot water may be taken as frequently as possible. In more severe cases, a stomach tube may be passed and the stomach thoroughly washed out. Should this fail to stay the vomiting, opium must be administered. But again in this instance it would be as well to have a further consultation with the surgeon, for such a condition as strangulation, possibly the original cause of the peritonitis, may have recurred a second time; or again, while one cause of obstruction has been removed, there may be another still present.

Food.—For the first forty-eight hours after operation, any food taken by the mouth will probably be vomited, and therefore rectal alimentation alone should be relied upon. At the most a little iced water may be sipped, more particularly in relief of the thirst which invariably occurs, but which gradually disappears with the adoption of rectal saline infusions. Nutrient enemata should contain peptonised milk, beef tea and eggs, and a little brandy, notwithstanding the more than doubtful question whether any of these substances become absorbed. But even assuming that no nourishment is gained in this manner, the mental effect produced by their administration quite justifies the proceeding. After thirty-six to forty-eight hours, if progress has been satisfactory, sips of milk or milk and water may be permitted, roughly speaking about 1 oz. every hour. When once the bowels have been opened, feeding by the mouth may be increased. Peptonised milk is the best form with which to begin, and other articles of diet are added gradually in order of their digestibility.

Should vomiting occur at any period during this administration of food, further food should be withheld, and in this contingency the substitution of ice will sometimes help to stay the thirst and vomiting.

The Mouth.—It is important that the mouth should be kept as clean as possible, and antiseptic proceedings should be instituted as soon as the post-operative shock has passed off. Mouth-washes of listerine 1 in 20 or glycothymoline will be found pleasant as well as efficacious.

Flatulence.—To prevent or to relieve tympanites a rectal tube should be passed for six or eight inches up the rectum four-hourly. If relief is not obtained an enema of turpentine may be given on the second day: tincture of asafœtida has been found similarly useful.

A hypodermic injection of eserine salicylate, $\frac{1}{100}$ gr. every four hours for six doses sometimes gives relief, but a careful watch must be kept for any signs of overdose. Intramuscular injection of 15 min. of pituitary extract = 0·25 gm. of gland substance or pituitrin repeated in one hour has also been recommended for paresis of the intestines. Occasionally hot flannels placed over the abdomen will lessen the distension.

The bowels should be opened after twenty-four hours preferably by small doses of calomel repeated at frequent intervals.

Hiccough.—A most distressing symptom which frequently occurs is hiccough. Generally speaking the more serious the patient's condition, the more intractable the hiccough, which is regarded as either due to the inflammation of the diaphragmatic peritoneum and consequent irritation of the terminal fibres of the phrenic nerve or to the absorption of toxins. The most efficacious treatment is counter-irritation of the epigastrium or along the course of the phrenic nerve in the neck. This is best achieved by the application of mustard leaves, which may be accompanied by massage of the neck. Inhalation of amyl nitrite has often proved of service.

Cocaine ($\frac{1}{20}-\frac{1}{50}$ gr.), turpentine and musk occasionally may prove of value.

If all other measures fail and hiccough is wearing the patient out through want of sleep, morphia must be employed.

Heart.—Throughout the post-operative treatment the heart's action must be carefully watched, and it may at any time be necessary to administer small doses of brandy or a hypodermic injection of ether ♏ x, strychine hydrochloride ♏ v, or camphor gr. iii. in olive oil ♏ x. A valuable cardiac stimulant in these cases is caffeine soda salicylate, $\frac{1}{4}-\frac{1}{2}$ gr. hypodermically, which can be repeated after six hours and later four-hourly if necessary. It is not to be recommended in children, since it often produces nervous symptoms such as insomnia.

Pain.—A certain amount of pain is to be expected after any abdominal operation, and there is no particular urgency in alleviating it. But should pain occur of such severity as to prevent all possibility of the sleep which is so essential in the early post-operative stage, recourse must be had to morphine, the only drug which is of the slightest value. Heroin hydrochloride, $\frac{1}{24}-\frac{1}{12}$ gr., is a useful way of administering it. It is well, however, to remember that pain may be due to vomiting, to tympanites, to a tight bandage, or even to a distended bladder, exigencies which do not call for morphine but for obvious appropriate treatment.

As the whole of the direction and application of the necessary post-operative treatment may be left entirely to the practitioner in charge of the case, and not to the surgeon who has performed the operation, it has been deemed advisable to describe these details. It is, however, outside the scope of this article to deal with the question of after-dressings.

Serums and Vaccines.—The fluid removed from the abdomen at the operation should be microscopically examined and cultures made with a view to discovering the causal organism, its relative abundance and, if subsequently desired, to the preparation of an autogenous vaccine. If an immediate microscopical examination of the peritoneal fluid can be made, the causal organism may be identified and a stock serum instantly employed. Thus the appropriate immune serum may be intraperitoneally or intravenously injected, whilst the patient is still on the table, a procedure which will naturally utilise the serum to best advantage. It is difficult to give any general rule as to the subsequent use of serum, but for the principles involved the reader is referred to the article on vaccine and serum treatment.

It is solely on this point of specific therapy that any distinction with regard to treatment in acute general peritonitis need be made—according to the micro-organism found. This may be one or more of the following: bacillus coli, streptococcus, staphylococcus, gonococcus, pneumococcus, tubercle bacillus.

Of these the two most important and frequent are the bacillus coli and streptococci which are considered below. Further details are to be found under puerperal septicæmia and tuberculous peritonitis, but staphylococcal, gonococcal and that fatal variety, pneumococcal peritonitis, are rare.

With regard to specific immunisation the choice of treatment will lie between the injection of serum, ordinary vaccine or sensitised vaccine.

As has been stated already, bacillus coli infection is by far the commonest, and in this case either anticoli serum or vaccine of coli bacilli (or sensitised vaccine) may be employed alone or in combination.

Should the infection be the result of coli in association with streptococci then antistreptococci serum vaccine or sensitised vaccine can be given in combination with the anticoli serum or vaccine of coli.

Antipneumococcal serum or pneumococcal vaccine, sensitised or not, is used in exactly the same manner as the above. When the use of vaccines has been decided upon it may be convenient at first to use stock vaccines, and later, if need be, an autogenous vaccine.

Sensitised vaccine in large doses of the infecting organism may be started at the time of the operation by first injecting the stock sensitised vaccine and following this up later by sensitised vaccine prepared from the patient's own organisms.

The sensitised vaccine has the double advantage that it produces no diminution (negative phase) in the patient's resistance and has a quicker action in raising the resistance than the ordinary vaccine.

In addition to these specific measures a general leucocytosis may be produced by the injection of sodium cinnamate, nucleic acid, etc., thus a great increase of leucocytes will be observed twelve hours after 50 c.c. of 2 per cent. nucleic acid are injected.

Acute Localised Peritonitis.—This will occur in all cases of inflammation of any abdominal viscus, and will be met with most commonly in such conditions as appendicitis, gastric and duodenal ulceration, abscess of the liver, salpingitis, and subphrenic abscess.

Peritonitis is not only merely a symptom of the underlying condition, but its treatment merges entirely into that of the cause which has produced it. The management of such cases is, as would be expected, very similar to the pre-operative stage of general peritonitis, and the treatment the physician will apply will be of an expectant nature in the hope that the inflammation will subside and not take such a course that surgical interference is certainly indicated. The reader must, however, be referred to the individual treatment of the separate sections. It would be impossible here to do more than remind the reader of the controversy, which even to this day is held regarding the justification of treating such conditions as appendicitis expectantly. A considerable consensus of opinion advises immediate laparotomy in all cases.

For the benefit of the other school we describe the expectant treatment that may be adopted. The patient must be put to bed and at first nothing should be given by the mouth except a little water or albumen water. When the

acute stage has passed milk and Benger's food are added. Hot fomentations should be applied to the painful region of the abdomen and often with advantage these may alternate with ice-cold applications. These will generally prove sufficient to relieve the pain, but in some cases it may be considered advisable to give aspirin 10 gr. or phenacetin 10 gr. by the mouth.

The use of opium has already been considered in the opening paragraphs.

No aperients of any kind should be given, but an enema should be administered, and this often materially assists in dispelling the symptoms. The best enema consists of 2 oz. of olive oil; large soap-and-water enemata may, by distending the bowel, convert a localised abscess into general peritonitis.

The pulse-rate and temperature must be carefully observed, at least every two hours, and an examination of the abdomen should be made at the same time. A leucocyte count should also be made at intervals. The patient must be kept in bed until all signs have cleared up.

With this expectant treatment improvement must occur or other measures will be necessary. As the symptoms subside an aperient, *e. g.* calomel, may be given and solid food gradually permitted.

Chronic Peritonitis

may be: (1) of the *adhesive* type, local or diffuse, occurring as the sequel of acute peritonitis or of previous tuberculous peritonitis; (2) of the *proliferative* type in which great thickening of the peritoneum and ascites occur; (3) peritonitis associated with *new growth* of the peritoneum; or (4) peritonitis associated with *tuberculosis* of the peritoneum.

For the first variety medicinal treatment is of little avail. Inunctions of mercury and the internal administration of iodide of potassium have been recommended. The symptoms which occur are most often due to some obstruction and interference with the mobility of the various viscera as the result of the adhesions formed, and only surgical treatment will give relief.

The treatment of ascites with cross references for the treatment of the various causes is considered below and embraces therefore the treatment of the second and third varieties.

Tuberculous Peritonitis

Tuberculous peritonitis exists in one of two forms: the exudative or ascitic variety, in which there is fluid present in the peritoneum, and the dry or adhesive. The two forms will be considered together below, attention being drawn to any points of difference in the treatment.

The general treatment is similar as regards habit and diet to that of patients suffering from tuberculosis elsewhere in the body. This includes as much fresh air and sunshine and the most hygienic surroundings possible. The patient should remain in bed so long as fever is present, and in any case as much rest as possible should be enjoined.

Diet.—The diet should be abundant and nutritious. Solid food is to be preferred, and, unless it causes indigestion, a slight excess of fatty food, such as cream, milk, butter, sardines and bacon, should be ordered.

The medicinal treatment resolves itself into two classes: (*a*) general and (*b*) specific. Of the two, present opinion advocates the latter, and results are so satisfactory that the writer considers it the only line of treatment which should be adopted. Before this method was introduced patients suffering with this disease were given $\frac{1}{2}$ gr. of iodoform dissolved in $\frac{1}{2}$ oz. of cod-liver oil three times a day after meals, whilst at the same time equal parts of unguentum iodoformi and cod-liver oil were rubbed into the abdominal wall twice daily. Another method was to apply to the surface of the abdomen $\frac{1}{2}$ dr. of unguentum hydrargyri, the anointed part being subsequently covered with a flannel binder. This medicinal treatment was sometimes accompanied by laparotomy, the indications for which are considered below in the description of the operation.

Tuberculin treatment consists in the injection of minute doses of tuberculin (TR). It is usual to begin in the ascitic cases with $\frac{1}{100,000}$ mg. and gradually to increase the dose until the temperature is subnormal. The injections are given at intervals of 2–5 days. This may take five or six weeks, generally less. Even when the patient at the end of this time appears to be cured the tuberculin injections must be continued for at least six months longer. In the dry form of peritonitis, tuberculin is occasionally not so efficacious, and in any case it is as well to begin with a much smaller dose. The amount usually employed is $\frac{1}{500,000}$ mg. and is very gradually increased. During the course of treatment with tuberculin, should there be any rise of temperature or complaint of pain, the injections must be temporarily stopped.

Laparotomy.—In view of the successful results obtained with tuberculin injections, laparotomy is not now so frequently performed, but it may be satisfactorily combined with either the drug or tuberculin treatment described above. In any case undue haste should never be displayed, and unless the accumulation of fluid distresses or shows signs of increase, at least four to six weeks' trial of medical treatment should be allowed before an operation is sug-

ted. On the other hand, operation must , be postponed too long, since it will be a)eless procedure if the patient has general)erculosis or develops tuberculous lesions)where. The operation consists in making incision in the abdomen so as to expose peritoneum. The ascitic fluid is allowed escape and the wound is closed, no drainage e being utilised. The value of this pro-ure is unquestionable, for improvement nost invariably follows. Some surgeons irri-e with oxygen into the peritoneal cavity at time of the operation (Gordon Watson). the majority of cases one operation is suf-ent to effect a permanent cure, but occasion-r a second operation is necessary, and in this er contingency it is well to explore for some us such as a caseating gland, etc., which y be removed at the same time. This thod of treatment is of most value in the itic cases, and may be unavailing in the esive variety. The treatment after the ration should be on the same lines as ore: fresh air, full diet, tuberculin, etc.

ymptomatic Treatment.—At any time during attack the patient may be troubled by niting, diarrhœa or pain.

Diarrhœa.—For this 10 gr. sodium citrate y be added to every half a pint of milk en. Should this not prove effectual, a cture of bismuth and chalk to which small es of opium, appropriate to the age, may be ed. Tannalbin, 8–15 gr., forms a useful iant. The same treatment will serve to y the vomiting.

For the *pain* the best relief will be obtained m Pulv. Ipecac. Co. given in graduated doses ording to age, allowing ½ gr. for each year, to a maximum of 15 gr. three times a day.

The *convalescence* of the patient is most im-tant and a holiday at the seaside or in the ntry is essential. The general health can built up and the anæmia cured by tonics h as cod-liver oil, iron and arsenic. For purpose syrup of iodide of iron or Syrup cerophos Co. are the preparations most quently employed.

Ascites

Ascites may be due to so many causes that scheme of treatment will be best considered ler the headings of *general,* which is more or applicable to all varieties, and *special* ere particular treatment is required according the cause.

General. *Habits.*—The patient must, if possi-, be kept in bed and the position which gives most ease is one in which the head and ulders are raised, since this does not allow fluid to press upon the diaphragm. In se cases which have been tapped or cannot for any reason be kept in bed, a binder or abdominal belt will give great comfort by its support.

Diet.—The amount of fluid should be gradually reduced so that the patient does not drink more than a pint or a pint and a half a day. During this process it is important to avoid causing great thirst or constipation which follow the restriction of liquids. A salt-free diet is usually advised in order to prevent the retention of chlorides. Farinaceous foods and vegetables produce fermentation and flatulence, and so must be prohibited. Irritating articles, *e. g.* pickles, spices, etc., should also be shunned and alcohol reduced to a minimum. A suitable dietary will include such articles as bread, butter, cream, milk, milky foods, junket, weak tea, eggs, fish, chicken, mutton.

The following treatment will be found the most effectual for the relief of the accompanying distension and pain—

1. *Antifermentative.*—All fermentable food must be forbidden and drugs administered which are credited with the prevention of fermentation. Guaiacol carbonate 3–8 gr., naphthalene tetrachloride 2–12 gr., or calomel $\frac{1}{20}$ gr. can be given three times a day.

2. *Carminatives.*—Ginger, cardamoms, tinctura carminativa, sodamint tablets or powdered charcoal are all useful. In more obstinate cases the following mixture may be tried—

Sp. Chlorof. ♏ xx
Sp. Am. Arom. ♏ xx
Sp. Cajuput. ♏ xx
p.r.n. ex aqua.

An attempt to disperse the fluid may be made by means of *purgatives, diaphoretics, diuretics* and *paracentesis.*

Purgatives.—Hydragogue purgatives are the most suitable and Pulv. Jalapæ Co. 30 gr. or magnesium sulphate up to 2 oz. are convenient. Another favourite remedy is to give two or three times a week the pill, Hydrarg. 5 gr. at night, followed in the morning by a Seidlitz powder or ½ oz. of magnesium sulphate.

Diuretics.—When the effusion is due to morbus cordis the only drug of any value is digitalis. In cases where the cause is not clear and there is no possibility of a renal origin, the following mixture may be of service—

Liq. Am. Acet. ʒ i
Sp. Æth. Nit. ♏ xx
Sp. Juniper ♏ xx
Inf. Scoparii ℥ i
Sig. t.d.s.

Other drugs such as copaiba, apocynum, etc., have their advocates.

Paracentesis Abdominis.—The indications for the performance of this operation are—

1. Dyspnœa, œdema of the lungs or pleural effusion, bronchitis, hæmoptysis, caused by the difficulty in breathing due to the peritoneal fluid.

2. When the amount of urine passed is scanty and is becoming progressively less.

3. When the fluid causes such distension that urgent relief of the pain is necessary.

4. When pressure by the fluid is evidently causing portal congestion with cardiac distress or severe hæmatemesis.

5. Signs of incipient delirium tremens or exhaustion.

The patient is propped up in bed, a many-tailed bandage is placed behind him. He must empty his bladder or a catheter is passed. The site of incision usually chosen is a point in the linea alba midway between the symphysis pubis and the umbilicus. If this point is dull on percussion the skin is prepared as for a surgical operation. A suitable trocar, one with a fine bore to prevent too rapid escape of the fluid and sufficiently long with a companion well-fitting cannula, is sterilised. A piece of rubber tubing is fixed to the cannula. It is pierced by the trocar in its passage into the cannula. In very nervous patients it may be advisable to freeze the skin or inject a local anæsthetic, but generally the instrument may be inserted without such preliminary. The trocar is then withdrawn through the hole in the rubber, which contracts and closes; the fluid then drains into a vessel placed at any convenient distance, pieces of strapping are placed over the cannula and a cradle is put over the patient, who is now left to drain. The fluid may run for as long as twelve hours; clotting in the tube may cause temporary cessation of the flow, which resumes if the clot be massaged along the tube. As the abdominal contents decrease the many-tailed bandage is gradually tightened.

When the fluid has ceased running, the cannula is removed and a collodion dressing is placed over the wound.

Half an ounce of brandy may be kept in readiness to administer if faintness occurs. There may be a little pain for the two ensuing days.

In malignant disease or in cases of recurring ascites an opportunity may be taken to inject an ounce of water containing 1 dr. of 1 in 1000 adrenalin chloride.

In recurring ascites operations such as draining the fluid into the crural canal by a bone bobbin (Gordon Watson) or omentopexy (Talma Morison) may be considered.

During paracentesis the accidents to guard against are—

1. Wounding a viscus.
2. Perforating a blood-vessel.
3. The introduction of septic matter.

Varieties of Ascites.—The special treatment required depends upon the cause.

1. *Cardiac.*—(See *Diseases of the Myocardium and Endocardium.*) The treatment will include absolute rest, purgation, diuretics, especially digitalis, but not *diaphoretics,* because of the heart failure they may induce. The following pills form convenient methods of administering—

Pulv. Digital. Foliæ gr. ss
Scillæ gr. ii
Pil. Hydrarg. gr. ii
(Matthew Baillie).

Pulv. Digital. Foliæ gr. i
Pulv. Scillæ gr. i
Calomel gr. i
Extr. Hyoscyami. gr. ii
(Guy's diuretic pill).

Digitalis can also be given with 5 or 10 gr. of diuretin or combined with 5 gr. of caffein citrate or with theocin sodium acetate 3 gr. Nativelle's granules of digitalin $\frac{1}{250}-\frac{1}{60}$ gr. are valuable. In those cases where digitalis is found to disagree strophanthus may be substituted for the digitalis.

2. *Renal.*—By renal dropsy is meant that due to acute nephritis and chronic parenchymatous nephritis. The dropsy which occurs in chronic interstitial nephritis is cardiac in origin and must be treated on those lines.

Diuretics must not be used, the kidneys must be spared as much as possible. Diaphoretics are permissible together with other means of stimulating the action of the skin such as hot-air baths, etc.

3. *Cirrhotic.*—(See *Cirrhosis of Liver.*)

4. *Syphilitic.*—(See *Treatment of Syphilis.*)

5. *Malignant.*—In this type it should be remembered that there is no advantage in restricting the patient's diet. A. S. W.

SURGICAL PRINCIPLES OF THE TREATMENT OF GENERAL PERITONITIS

Early diagnosis and early surgical intervention are admittedly the most important factors in successful treatment. With regard to diagnosis let it be admitted that it is not in the power of any man or body of men to diagnose the presence of early general peritonitis in the lower abdomen; the onset of peritonitis in the upper abdomen is usually accompanied with such grave changes that it can hardly be diagnosed, but in the lower abdomen, where it most frequently originates, only too often its early symptoms are masked. In children it may be observed that rigidity of the abdominal wall is a most deceptive symptom. Over and over again I have opened the abdominal cavity and found it full of septic fluid where there was no abdominal rigidity at all before. In children

the facial expression in my experience is least likely to mislead.

If the term "localised appendix abscess" had no place in our mental view there is no doubt many valuable lives would be saved.

Let it be clearly understood, for the same reason, that the man who decides in favour of immediate operation in every case where he is doubtful of his own diagnosis will never have reason to regret his decision.

Having decided on operation, no time should be lost, the patient should be kept still and in a sitting posture to avoid gravitation of septic fluid to the upper abdomen.

The lightest possible degree of anæsthesia should be used, in order not to add to the patient's vomiting and to the amount of poisons already circulating in his blood. There can be no doubt that spinal anæsthesia is of great use in these cases. Two points of vital importance in the operation are rapidity of operating and doing as little as possible to disturb the intestines. The search for a gangrenous appendix should be short, and if rapidly found it should be simply clamped, ligatured and divided, and a large tube pushed down towards its original position.

The largest obtainable rubber tube with lateral openings is then pushed down to the bottom of Douglas' pouch and a wick of gauze placed inside it and the wound closed rapidly.

No attempt should be made to clear lymph off the intestines—it is nature's protection and should be respected as such—all are at present agreed that it is equally unwise to disturb the folds of small intestine or attempt at all making what was once called "the peritoneal toilette"—drain thoroughly and leave the rest to nature should be our motto. It should not be imagined from this that our resources are now at an end—far from it. There is no surgical complaint where close attention and after-treatment can do more to win the day.

The patient should be put back in bed in a sitting position and kept in that position until all immediate danger from spreading of sepsis is at an end. The first endeavours made are to combat shock and continued septic absorption. Whatever be the cause of shock its treatment is now sufficiently clear. "Diffusible stimulants," ether, strychnine, hypodermic injections of alcohol and the like are all useless. It is fairly certain that in the condition of shock the system is "bled into the abdomen." Where the great veins of the splanchnic area are dilated the systemic circulation wants fluid and must have it, and this very physical need of fluid to maintain the circulation is of use in diluting the toxins in the blood. The rapid and dangerous method of intravenous injection is now discredited and abandoned. Fluid should be given into the loose tissues of the axillary flanks and buttocks through a needle from a Thermos flask at 104° F., one pint to one and a half pints at a time and repeated as often as the local swelling is absorbed, until the patient has passed beyond the first profound danger of shock. The fluid to be injected may be normal saline solution prepared from boiled water by the addition of B. W. & Co.'s tabloids, or a pint of 5 per cent. glucose may well be given, this being prepared in the same way; recent work would suggest that this is preferable. If there is need for subcutaneous injections at all, remember that they should be begun *before the patient has left the operating table.* Fluids can also be administered by continuous slow administration by the rectum through a small (No. 6) rubber catheter passed some six inches. The fluid is allowed to run in drop by drop, each half pint taking half to three-quarters of an hour to run in, and being steadily absorbed. The apparatus for performing this simple nursing detail (honoured by the proctologists as proctoclysis, a name suggestive of Mesopotamia) is well known. It should be clearly recognised that this procedure can only replace the steady drainage of fluid from the peritoneum. It is useless to combat against shock, and there are many persons who cannot tolerate or retain any fluid by the rectum (55 per cent. in children). It is my practice to employ it after all serious abdominal cases and more especially after all cases so long as there is a drain into the peritoneal cavity.

Within six to twelve hours of the operation our hope will be that the patient can take some fluid by the mouth. An attempt should be made with this *as soon as the patient asks for it* (a rule worth remembering), and, if successful, fluids should be steadily pushed. I never allow a patient in such case to be pressed to take fluids, and my experience is that if they ask for fluids they will not as a rule vomit them (always provided that there is free peritoneal drainage). The character of the fluid can be rapidly changed—begin with ice water, lemon ice water, lime ice water, iced barley water, iced albumen water, iced sherry whey water, iced clear soup or beef tea.

The next condition which will absorb our attention is that known as ileus or paralytic distention of the intestine or popularly "the wind." Once well established this is highly dangerous and may actually kill the patient with all the symptoms of acute intestinal obstruction. The moral in its treatment is prevention. Each surgeon has his own ideas as to prevention and treatment. In a short article like the present I can only give my own. I attach importance to the following—

1. Maintenance of the sitting-up posture.

2. Early and plentiful administration of fluids.

3. And, most important, continued hypodermic injections of pituitary extract (one vaporole, B. W. & Co.). It is my custom to give the first injection before the operation is over and repeat the injection every four hours for the first twenty-four hours, every six hours for the second twenty-four hours, stopping the injections if there is a satisfactory action of the bowels. Pituitary extract has a double effect, it increases the blood pressure and, more especially, it stimulates the muscular coat of the intestine.

4. Attempts should be made as early as possible to empty the intestine as a routine. I give one ounce of castor oil eighteen to twenty-four hours after the operation (I am convinced it is most unwise to delay it to a later time); in three hours this is followed by a turpentine enema—this is repeated in two hours if there is no result—and then 5 gr. of calomel are given; this is repeated in 1 gr. doses every three hours until 10 gr. have been given, a turpentine enema being given *before* each fresh dose of calomel and the calomel discontinued if there is a satisfactory action.

If the calomel does not act stronger purgatives should be given. I well remember one case which seemed hopeless and was rescued by 30 gr. of Pulv. Jalapæ Co. I have also given Croton Oil 3 min. The general opinion of nurses at the present time is that the continuous injections of pituitary extract make their task in relieving the bowels much easier. I believe that this is true.

It may be considered that once distension is relieved and the bowels properly opened immediate danger from septic peritonitis is at an end; and with regard to later complications we are not concerned here.

One last word. No case of acute septic peritonitis should be regarded as hopeless. Close by is certain death with outstretched hand, and shall the surgeon pause and leave the patient in that inevitable grasp? Even if the patient dies on the table I maintain he should have the chance of life given him. It is impossible to say that any case is hopeless; both in children and in adults I can reckon on a few recoveries in patients who were pulseless and *in extremis*—surely, therefore, the operation must in all cases that are just alive be undertaken, boldly and rapidly, whatever the risks.

J. K. M.

VISCEROPTOSIS

The normal position of the viscera and its maintenance in different postures depend upon (1) the proper development of the thorax, and (2) the maintenance of the normal intra-abdominal pressure.

Insufficient development of the thorax is not infrequently congenital; it may also result during the period of growth from disorders of nutrition, thoracic diseases and from insufficient exercise. As the thorax is long and shallow, the thoracic part of the abdomen is abnormally small, and the liver, spleen and kidneys, and the part of the stomach which is normally hidden beneath the ribs, together with the colon, are displaced downwards.

The most common cause of visceroptosis, however, is a diminution in the intra-abdominal pressure. The viscera are normally kept in position by the slight positive intra-abdominal pressure, which is maintained by the tonic contraction of the muscles of the abdominal wall and the pelvic floor, their peritoneal attachments remaining slack. The position of the diaphragm also depends in part upon the difference between the negative intra-thoracic pressure and the positive intra-abdominal pressure; if the latter is reduced for any reason, the diaphragm and the organs which are attached to it descend when the vertical position is assumed. A fall in intra-abdominal pressure is most commonly due to weakness of the abdominal and pelvic muscles. Even when the abdominal and pelvic muscles are strong, the diminution in the bulk of the abdominal contents by the disappearance of the normal intra-abdominal fat, when for any reason a condition of emaciation develops, results in a fall of intra-abdominal pressure and consequently in visceroptosis.

When the contents of the thoracic abdomen are displaced downwards owing to its insufficient development, the viscera drop no more than those of normal individuals on assuming the vertical position. When, however, visceroptosis is due to low intra-abdominal pressure the viscera drop as soon as gravity comes into play, but at first they regain their normal situation as soon as the patient lies down. At a later stage, when the daily descent of the viscera has continued for a considerable time, the displacement persists in the horizontal position.

The symptoms present when visceroptosis is due to an ill-developed thorax are not caused by the ptosis, but by the general condition of malnutrition which is frequently present. It is therefore only necessary in this place to discuss the treatment of the form of visceroptosis which is due to low intra-abdominal pressure.

Prophylaxis.—Much can be done to prevent visceroptosis and the associated constipation in women by proper management of the puerperium. The patient should remain in bed fo

the first twelve or fourteen days after parturition, or, when much bruising has occurred, especially in the case of primiparæ, for as long as three or four weeks. The first few days after getting up should be spent for the most part on a couch, and a return to full physical activity should only be permitted after about six weeks.

Treatment.—Visceroptosis due to insufficient development of the thorax requires no special treatment. In all other cases the first indication is to raise the intra-abdominal pressure. In order to do this the condition of the abdominal and pelvic muscles must be improved. Exercise and Swedish gymnastics are of great value; massage and faradism are less useful.

It is essential to prevent the over-stretching of the muscles, which occurs as soon as the erect position is assumed, as it is impossible for them to regain their normal tone so long as they have to bear the weight of the viscera for the greater part of every day. In almost all cases, therefore, an abdominal support is required. It has sometimes been taught that a support should only be worn when the abdominal muscles are so weak that their recovery is deemed unlikely, as improvement in the condition of the muscles is supposed to be rendered impossible by the disuse-atrophy, which the support is believed to cause. This view is, however, erroneous; by relieving the abdominal muscles of the weight of the viscera, a support prevents them from being stretched, with the result that they generally regain much of their former strength. A support, moreover, often gives so much relief to the abdominal discomfort caused by visceroptosis that it enables a patient to eat more without fear of discomfort and to take more exercise, and so indirectly helps to overcome the sluggish action of the intestines, which may be present in addition to the dyschezia generally present as a result of the weakness of the abdominal muscles.

An abdominal support should fit closely to the symphysis pubis and Poupart's ligaments below; above it should not extend higher than the umbilicus. It should be so made that it presses the abdominal contents upwards, backwards and inwards. It is essential that it should fit well and cause no discomfort. In mild cases of visceroptosis in women all that is necessary is a special straight-fronted corset, which does not constrict the waist, but supports the lower part of the abdomen. In most cases, however, a light support hinged in the middle line and fixed in position by steel springs passing over the hips to end in pads applied to the sacrum is required. In severe cases, especially in very thin patients, a pneumatic pad should be fixed under each side of the support; this can be inflated with a pump by the patient, the degree of inflation being reduced as improvement occurs and the patient becomes stouter. Only in exceptional cases should a support be used with the object of supporting a single organ; I have several times seen a kidney pad produce serious digestive disturbances by pressing upon the colon or stomach, often without effectively holding the kidney in position. An ordinary visceroptosis support is sometimes all that is required to keep a movable kidney in position, but it may be necessary to have an extension with or without a pad added to the support.

The abdominal support should always be put on when the patient is lying down with the pelvis raised, so that the organs are held in proper position, and it should be worn all day. Not infrequently, however, the X-rays show that the stomach and colon drop on standing almost or quite as far when the support is worn as without it. This is particularly likely to be the case when an organ falls into the true pelvis, as the support does not then reach low enough, and in thin patients, upon whom it is impossible to exert sufficient pressure. In such cases, indeed, I have sometimes found with the X-rays that the support actually holds the organ down and prevents it from rising when the horizontal position is assumed. In numerous instances I have found that a support does not hold the colon or stomach up at all and yet the patient derives great benefit from wearing it. This shows that it acts chiefly by increasing intra-abdominal pressure, and that many of the symptoms ascribed to kinks are really the result of the low intra-abdominal pressure interfering with the circulation and with the proper performance of defæcation. It has, for example, been frequently said that mild cases of the so-called "ileal kink" can be relieved by the mechanical effect of an abdominal support which holds the cæcum up and prevents its development. No radiographic evidence, however, has ever been published to show that it does this, and my own radiographic observations show that nothing will hold a cæcum out of the pelvis, which remains there on lying down, and that it is even rare for a support to hold it out of the pelvis when it only falls from the right iliac fossa on assuming the vertical position. The effect of the support is thus general and not local in a large majority of cases.

When visceroptosis is due in part to weakness of the pelvic floor this may require treatment by pessaries and local operations, which have the object of restoring the injured parts to a more normal condition.

In slight cases of gastroptosis the patient should lie down for an hour after meals, but in severe cases of visceroptosis, in which there is great emaciation or the abdominal muscles are greatly atrophied, it is best for the patient to remain in bed for some weeks, as by this

means the intra-abdominal pressure is reduced to a minimum and all tension is removed from the abdominal and pelvic muscles; the foot of the bed should be raised as high as possible, as this helps the organs to return to their proper position, which is often maintained after the patient gets up again, especially if he gains weight during the rest.

As most patients with visceroptosis are thin they should be given a generous diet, as an increase in the amount of intra-abdominal fat helps to keep the viscera in position. The meals should be frequent and small in bulk, fluids being given apart from solids in order not to distend the stomach.

It is very important that a proper squatting attitude should be assumed during defæcation, and if a patient has an abdominal support he should wear it during the act. The dyschezia should be treated by graduated enemata (*vide Constipation*), until the muscles of defæcation have regained their strength.

Only in exceptional cases should any operation be performed for fixing dropped viscera. As one organ is rarely dropped alone, the effect of such operations is rarely permanent, and the neurasthenic condition of many of the patients makes surgical interference of any kind most undesirable. The chief exception to this rule is in cases of movable kidney, in which serious symptoms have resulted from obstruction of the ureter or blood-vessels and an abdominal support has not given complete relief. Short-circuiting operations are very rarely required for the purpose of overcoming kinks in the alimentary canal. Gastro-enterostomy is never followed by any improvement in cases of gastroptosis, but in rare cases of severe kinking at the splenic flexure a short-circuiting operation, such as an anastomosis between its limbs, may be required, and the results obtained are generally satisfactory. A. F. H.

DISEASES OF THE PANCREAS

There are two main sources of difficulty in treatment of diseases of the pancreas, one the difficulty in diagnosing all but the most obvious lesions of the gland, the other its comparative inaccessibility, approached as it is through a viscus with an acid secretion, whereas its own is alkaline.

Methods of diagnosis are not included in our present survey. I propose in the first place to lay down certain considerations which govern the treatment of pancreatic diseases in general, and then the details appropriate to special conditions.

1. *Dietetic Treatment.*—Pancreatic juice contains ferments which are capable of acting on all foodstuffs and is the only one able to split fat to any extent, the lipolytic power of gastric juice being of academic rather than practical interest. It therefore follows that when the pancreas is diseased, fats are badly borne, for not only are they lost, excess of unsaponified fat appearing in the stools, but by coating over the proteins they hinder their absorption and increase their putrefaction. Proteins are digested by pepsin and can therefore be given so long as a form is chosen in which they can be acted upon rapidly in the stomach, such as minced meat. Certain proteins like caseinogen can also be digested by the erepsin of the succus entericus, and can therefore be used, *e. g.* plasmon or protene, whereas egg albumen will not. In addition the relatively large amount of sulphur contained in eggs renders them very prone to putrefactive changes. Gelatin on the other hand, owing to the absence of aromatic amino-acids, is not so liable to these changes, and can replace proteins to a limited extent.

For the digestion of starch we have to rely upon the ptyalin of the saliva; it follows that to take advantage of this, starchy foods should not be given in a soft form such as ground rice, but in a dry crisp form like toast, biscuit or rusk, which, requiring thorough mastication and insalivation, reaches the duodenum already largely digested. Sugars like glucose can be absorbed without further digestion, while cane sugar, maltose and lactose can be digested by the succus entericus. But their use in pancreatic diseases is unfortunately limited by the diminished sugar tolerance often found. The limit of carbohydrate tolerance should therefore be determined in the way described under diabetes.

2. *Regulation of the Pancreatic Secretion.*—The acid of the gastric juice is the great stimulant to both the external and internal secretion of the pancreas. Accordingly, if it is deficient it should be reinforced by the administration of dilute hydrochloric acid, or better 15 gr. tablets of betain chloride (acidol) freshly dissolved in water after meals. This liberates nascent hydrochloric acid slowly in the stomach. On the other hand, hyperchlorhydria over-stimulates and finally exhausts the pancreas, thus helping to set up chronic pancreatitis. It should therefore be corrected by alkalies, including magnesia, after meals.

3. *Supply of Deficient Ferments.*—This presents difficulties. The simplest method would be to pancreatise the food before administration, but this is liable to impart a bitter, disagreeable flavour. If ferments are given with the idea of their acting when the duodenum is reached, they will be destroyed in the stomach unless enclosed in capsules capable of resisting gastric digestion, and then we can feel little certainty that they will be set free in the duodenum.

Keratin-coated capsules are supposed to be the best. Capsules of gelatin toughened in formalin are apt to escape undigested even in the healthy subject. Takadiastase has been given before meals for the digestion of carbohydrates. One or more $\frac{1}{4}$ gr. tablets of pankreon with meals may be given a trial. Holadin is said to contain all the external and internal secretions of the gland. As it has been repeatedly demonstrated that the internal secretion of the pancreas cannot be absorbed by the intestinal mucosa the advantage of its addition is problematical. It is given in capsules. Stockton states that he has been unable to convince himself that any such ferments produce any improvement in the general condition of the patient or in the stools. He adds that many preparations on the market are practically inert, and many combinations are self-destructive, provided they are made as described.

4. *Disinfection of the Pancreatic Ducts.*—There are two drugs which are known to be excreted by the pancreatic ducts, as well as by other channels. These are helmitol and aspirin, both of them disinfectant in action. Routine employment of them in doses of 5 to 20 gr. three times a day is therefore a rational procedure and should be given a thorough trial. But perhaps the most efficient means of ridding the pancreatic ducts of infection is to drain them by a cholecystostomy, which, if indicated, should not be too long delayed.

5. *Diminution of Intestinal Putrefaction* resulting from diminution or absence of the pancreatic juice. The dietetic factors in these conditions have already been considered. The value of sulphates is not confined to their aperient action, for by combining with putrefactive bodies they render them inert. They should not be given in a concentrated form for this purpose as they are then apt to provoke desquamation of the intestinal mucosa, thus facilitating the absorption of toxins. Small doses of calomel, boric acid, β-naphthol or naphthalene tetrachloride in 5 gr. capsules may all be given a trial.

Any chronic disease of the pancreas, accompanied by insufficiency of its secretion, will call for some or all of these methods of treatment.

Pancreatic Infantilism

Any chronic disease in a child may cause persistent infantilism. Rarely the pancreas is responsible, as in a case reported by Byrom Bramwell, in which the exhibition of a glycerine extract of the pancreas checked fatty diarrhœa and promoted growth. It is difficult, however, to be sure that this is not the same condition as that described by Herter as due to chronic intestinal infection and characterised by an overgrowth and persistence of the flora of the nursling period. Intestinal disinfectants are therefore also indicated.

Acute Pancreatitis

1. **Hæmorrhagic.**—This terrible condition is naturally very unfavourable for treatment. Even morphia may not be able to relieve the pain. The general view is that as operation may increase the shock, it should be delayed in the hope of the patient surviving until the more amenable stage of gangrene is reached. Bosanquet points out, however, that diagnosis is rarely possible on clinical grounds and that the conditions with which it may be confounded, such as perforation of the stomach, duodenum, or gall bladder and intestinal obstruction, are all such as to demand operation. And as he is able to show a recovery rate of 29·6 per cent. after operation, there is considerable force in his contention. Billington and Goodwin advocate the simultaneous performance of appendicostomy so that large quantities of saline can be introduced into the colon, but in view of the shock, anything which prolongs the operation is to be deprecated. Self-digestion may occur along the track of the incision into the gland, and should be met by smearing the edges of the wound with antiseptic ointments and by plenty of porous packing. Pawlow adopted this method in his experimental animals, after noting that the animals themselves kept the wound in contact with sawdust or even with plaster they had scratched from the walls. Otherwise the after-treatment is that appropriate to any laparotomy.

2. **Suppurative and Gangrenous.**—Every one is agreed that here the indications are for immediate operation. In Bosanquet's series of thirty-five cases operated on, the mortality was thirteen, giving a recovery rate of about 63 per cent. Ten cases not operated on all died.

3. **Pancreatic Mumps.**—This is the only benign form of acute pancreatitis. Its recognition is important lest it should be taken for one of the graver forms requiring operation. It is usually preceded by parotitis, when its nature will be clear; but exceptionally, like the orchitis of mumps, it may occur before the swelling of the parotids. The pulse tends to be slow, which distinguishes it from other forms of acute pancreatitis. Glycosuria hardly ever occurs. It lasts only a few days and the prognosis is good. It should be treated by rest in bed, hot applications to the abdomen, light diet and cooling demulcent drinks, such as barley-water flavoured with lemon. Morphia may be required. Strong purgatives are contra-indicated.

Chronic Pancreatitis

Alcoholism, syphilis and arteriosclerosis are factors in producing chronic pancreatitis, which

must be taken into account in its treatment. Glycosuria must be looked for at frequent intervals and treated dietetically if present. The general lines of treatment previously laid down apply particularly to chronic pancreatitis. Cammidge considers that if there is not definite improvement after a month's course of aspirin and helmitol, the operation of cholecystostomy should not be deferred. This seems a better operation than cholecystenterostomy, as any infecting agent escapes from the body and is not returned to the intestine, whence it might again ascend the pancreatic duct. If the bile escaping from the gall bladder contains a pathogenic microbe a vaccine prepared from this should be tried. The biliary fistula should be kept open for at least six weeks.

Pancreatic Calculi

The flow of pancreatic juice may be stimulated by drinking freely of water acidified by CO_2, or a dilute acid which increases the formation of secretin, the hormone to pancreatic juice. In this way it may be possible to wash out small stones, but these are less likely to be diagnosed. Injections of pilocarpin would have the same effect, but are more risky and are not to be recommended. Pancreatic calculi have been successfully removed by operation.

Pancreatic Cysts

The only treatment is operation by incision and drainage as soon as the diagnosis has been made. If postponed, troublesome adhesions may form, or there may be intracystic hæmorrhage, suppuration or extensive fat necrosis. Healing is usually slow and a fistula may result. Exploratory puncture or an attempt to remove the cysts is to be condemned. A consecutive glycosuria may call for treatment.

New Growth of the Pancreas

Operation is only possible where the head of the gland is not involved, and this is rarely diagnosed. The diet suitable for pancreatic disease in general should be given. Anodynes may be required externally and internally. The pruritus can be treated as described under *New Growth of the Liver*. Bosanquet suggests cholecystenterostomy to short-circuit the bile for the relief of pruritus. If an exploratory laparotomy is performed, this certainly might be done. The consequent disappearance of the jaundice has a good mental effect on the patient.

W. L. B.

DISEASES OF THE LIVER, GALL BLADDER AND BILIARY DUCTS

1. **Treatment of Catarrhal Jaundice.**—During the initial stages the patient should be confined to bed on account of the vomiting and the liability of the catarrhal process to spread. Calomel in ½ gr. doses every hour until six doses have been taken is considered the best treatment for the vomiting, though the occasional intolerance of some patients to this drug has to be remembered. It has the additional advantage of being aperient without causing drastic purgation, which should be avoided. Its cholagogue action is purely indirect, as anything which stimulates peristalsis of the intestines causes peristalsis of the bile passages also. Ten hours after beginning the calomel treatment, a Seidlitz powder should be given, for repeated doses of calomel, which are not effective in getting the bowels open, may easily set up mercurial stomatitis. Alkalies are indicated as solvents of mucus, and, if the vomiting persists, should be combined with bismuth salicylate. The following formula is a useful one—

Bismuthi Salicylatis gr. x
Sodii Bicarb. gr. x
Sp. Menth. Pip. ♏ x
Sp. Chloroformi ♏ v
Inf. Rhei ʒ ii
Inf. Gent. Co. ad ℥ i
Quartis horis.

As soon as the state of the stomach permits, the more active sodium salicylate should be substituted. The value of salicylates is twofold: they dilute the bile and help to disinfect it, being partly excreted by the bile ducts. The diet will naturally be light. Milk is usually recommended as the mainstay, but owing to its comparative richness in fat it is not really suitable and is often much disliked by the patient. I prefer to give barley-water flavoured with lemon, with the white of an egg and a teaspoonful of somatose or plasmon to each half pint. Tea is usually forbidden, though it is difficult to see on what grounds; jaundiced patients often crave for it, and, if made in the Russian fashion without milk, but with a slice of lemon in it, seems free from objection. If the practitioner feels reluctant to abandon milk, it should be separated or thoroughly skimmed to get rid of as much fat as possible, and then a grain of sodium citrate added to each ounce of milk to diminish curdling. Benger's Food, calves' foot jelly and lemon sponge are pleasant and can usually be taken without difficulty. Mineral waters of an alkaline type, like Vichy, Apollinaris or St. Galmier, may be drunk freely.

When the bile pigment has returned to the fæces, the patient feels much better, though still jaundiced; he can now get up and the diet should be cautiously increased. There is sometimes considerable depression during convalescence, for which strychnine and calumba may be given. Dilute nitro-hydrochloric acid, in

10 min. doses, is often recommended, but should not be given until all signs of obstruction have passed off. It may be noted that, apart from the inconvenience of the discoloration by bile pigment, the disagreeable symptoms are mainly due to bile salts in the circulation, which are responsible for the headache, depression, slow pulse and pruritus. The treatment of this last symptom is dealt with fully under *New Growth of the Liver*.

2. Treatment of other Forms of Jaundice.—Here the treatment depends upon the cause. In the new-born the slight "physiological jaundice" calls for no treatment. Severe jaundice of the new-born depends on septic infection of the umbilical vein, hereditary syphilis or congenital malformation of the bile ducts. The first calls for vigorous, though usually unavailing, treatment of the septic focus; the second, for antisyphilitic remedies; while, for the last, nothing can be done. It is hardly likely that the child could stand an operation even for a simple occlusion of the main duct, and the condition is often more complicated.

Obstructive jaundice in the adult may be due to gallstones and their results, cancer of the liver, bile passages, or head of the pancreas, and exceptionally to other forms of pressure from without. The treatment of each of these will be found under the appropriate headings. The possibility of parasites in the bile ducts must be borne in mind. Toxæmic jaundice occurs in certain specific fevers, with poisons such as phosphorus, arsenic and snake venom, and in various other conditions exciting catarrh of the smaller bile ducts. The treatment of the graver forms is as for *Acute Yellow Atrophy*. True hæmolytic jaundice is met with in the acholuric family type, in which there is undue fragility of the corpuscles. Splenectomy has been performed with good results. Epidemic catarrhal jaundice is treated on the same lines as the sporadic cases.

3. Acute Yellow Atrophy.—In the early stages the case will be treated as catarrhal jaundice; the patient should be encouraged to drink large quantities of barley-water and the like. With the onset of severe symptoms it is advisable to purge freely and to give saline infusions intravenously, or into the loose cellular tissues; as much as three pints may be given at about the rate of a pint an hour. The diuretic effect of the infusions may be increased by adding a drachm of sodium acetate to each pint of saline. Venesection has the advantage of removing the toxins while the infusion is diluting them. Theocin-sodium acetate in 2 gr. doses every four hours is a useful diuretic. Gastric sedatives, such as bismuth subnitrate, cerium oxalate up to 5 gr. every four hours, carbolic acid in 1 min. doses mixed with 2 dr. of water, at frequent intervals, or 1 min. of Tr. Iodi in 1 dr. of water every ten minutes, may be required for the distressing vomiting. As carbohydrate is the foodstuff most easily metabolised in this state, and as it appears to help the antitoxic action of the liver, dextrose should be given by the mouth or by the rectum, or, if necessary, with the intravenous saline; a suitable strength is 2 per cent. if sodium acetate is also given, 4 per cent. if it is not. On the analogy of puerperal eclampsia, morphia may be found useful for convulsions and delirium. Chloroform inhalations should not be given for the convulsions because of their toxic effect on the damaged liver.

Hollaender suggests that Freund's method of treating eclampsia by injection of the serum from healthy pregnant women should be tried for the acute yellow atrophy of pregnancy. It is to be feared, however, that the prognosis remains extremely grave whatever method of treatment may be adopted.

4. Treatment of Gallstones and their Results.—Gallstones are due to infection of stagnant bile by the B. coli, B. typhosus or, occasionally, some other organism. They are commonest in stout, middle-aged women, in whom all the conditions favourable to stagnation of the bile are present, for the outflow of bile largely depends on peristalsis and the movement of the diaphragm as well as on the rate of secretion. Constipation, sedentary habits, drinking too little fluid and tight-lacing will, therefore, all contribute to stagnation. Two cases of gallstones I have seen in patients under thirty were both in grossly and prematurely stout women who had obviously tight-laced to an extreme degree. Visceroptosis is an important factor, for it favours both constipation and infection of the bile ducts. Its greater frequency in women is probably largely responsible for their greater liability to gallstones.

Gallstones may remain latent in the gall bladder, causing no symptoms beyond hyperchlorhydria due to reflex spasm of the pyloric sphincter, attacks of flatulence and a deep-seated tenderness on pressure under the right costal margin when the patient bends forward, or tenderness in the right sub-scapular region. The presence of a zone of hyperæsthesia somewhere between the costal margin and the umbilicus on the right side in a patient with acid dyspepsia is suspicious of gallstones. Typhoid "carriers" will generally be found to be the subjects of gallstones.

The passage of the gallstones into the bile ducts produces an attack of hepatic colic. The pain may be so agonising as to make it advisable to give a few whiffs of chloroform before proceeding to further treatment. Then

a hypodermic injection of morphine tartrate, $\frac{1}{4}$ gr., should be given, with the addition of atropine sulphate, $\frac{1}{100}$ gr. This combination helps to dilate the bile ducts to their fullest extent, thus diminishing the colicky contractions while facilitating the onward passage of the stone. The dose may have to be repeated. I am accustomed to follow this up with 10 min. doses of tincture of belladonna every four hours, until the patient is fully under its influence. The addition of salicylate of soda in 10 gr. doses helps to dilute the bile as explained above, and on several occasions I have been rewarded by the passage of stones after this treatment. Hot applications, of which antiphlogistine is one of the most convenient, are grateful to the patient. Bain recommends mustard packs over the gall bladder.

Between the attacks treatment is directed towards regulating digestion and checking the formation of stones as far as possible. Dyspepsia is usually of the hyperchlorhydric type, combined with intestinal flatulence. Treating the hyperchlorhydria relieves some of the symptoms, but will not help to cure the patient, as it is due to a spasm which is protective in origin. The dietetic principles underlying treatment are that meat extracts, purins and condiments help to produce hyperchlorhydria; soft carbohydrates and green vegetables promote flatulence. The fats, while diminishing the secretion of acid in the gastric juice, depend on bile for their absorption, and if not absorbed they increase intestinal putrefaction by coating over the proteins; moreover, their influence in producing obesity must not be forgotten. The practical deductions from these considerations are: (1) white fish, eggs, cheese, mutton and chicken may be allowed, while soups, broths, liver, kidney, sweetbread and rump-steak should be forbidden until the hyperchlorhydria is checked. (2) Dry forms of carbohydrate, such as biscuits, rusks and toast, are preferable to bread, ground-rice puddings and the like, because they demand thorough mastication before they can be swallowed, and, therefore, undergo a considerable degree of digestion by the saliva. (3) Sweets can be selected from jelly, egg custard, omelette, junket and stewed fruit. (4) At first vegetables had better be barred altogether, for, though cellulose is an aid to peristalsis, it promotes flatulence. As the patient's intestinal condition improves this rule may be gradually relaxed. (5) Fats, in the form of butter, cream or fat meat, should only be allowed in small amounts, for the reason given above.

It is important that water should be drunk freely to prevent inspissation of the bile. Patients do not care to be told to drink water from the tap, preferring, as of old, the waters of Abana and Pharpar. It is well, therefore, to select a spring which is mildly aperient, slightly alkaline, and not too highly mineralised, such as Rosbach, Apollinaris, St. Galmier, Vittel (*source salée*), or Evian. The sulphur waters of Harrogate are recommended by some. Salutaris water has the advantage of not being mineralised at all.

As to drugs, calomel once a week, alkalies and salicylates may be used to advantage as in catarrhal jaundice. Urotropin and salicylates are both disinfectants which are excreted by the bile; as is also helmitol, a derivative of urotropin which can act in an alkaline medium. A course of these drugs is advisable in all cases. Bile salts are cholagogues and are often recommended, but I have not been much impressed by the result of their administration. In any case, it is important not to give them while there is still an obstruction to the duct, as this would merely add to the amount of bile salts in the circulation and thereby increase the headache, depression, pruritus and bradycardia. A convenient preparation of bile salts is the colalin tablet, containing $\frac{1}{8}$ to $\frac{1}{2}$ gr., which may be given three times a day, or, if preferred, the colalin laxative tablet may be substituted. The treatment of pruritus is dealt with under *New Growth of the Liver*.

It is difficult to believe that any drug has a directly solvent action on gallstones. As the stones are said to dissolve in normal bile, the restoration of a healthy secretion is the best, if not the only way, of effecting this. Large doses of olive oil were formerly administered with that object, because gallstones were thought to crumble in this medium. It is true that fatty concretions may be passed when large doses of olive oil are given, but these are merely calcium and magnesium soaps, which might be formed by any one thus treated. And olive oil can hardly be suitable treatment for obesity. Crumbling of a stone can only conceivably be induced if it were protruding from the ampulla of the duct into the duodenum. Yet it is not likely that the treatment would have had such a vogue if it never did any good. I suggest that it alleviated symptoms of hyperchlorhydria by inhibiting gastric secretion. But there are other methods of doing this without its disadvantages.

Many surgeons are in favour of operative treatment in all cases of diagnosed gallstones, maintaining that one never knows when serious complications may occur, which would render operation inevitable and, at the same time, more difficult. Such grave views are hardly justified and probably originate in surgeons chiefly seeing the more serious cases. It is said that gallstones may form again after operation,

but it is more likely that all the stones have not been removed from a loculated gall bladder. It must be admitted, however, that medical treatment should not be too prolonged if the patient is not definitely improving. The chronic irritation of gallstones may set up cancer of the gall bladder. Bain's view is that, if there is no diminution in the objective signs after three weeks, immediate operation is advisable, while, if progress is not marked during the next three weeks, surgical interference is indicated. This is a practical rule to work by, but, as he says, "the frequency of operations for gallstone disease is a distinct reproach to medicine," implying that earlier and more efficient medical treatment would reduce the number.

It will be generally agreed that recurrent effects of gallstone colic and septic complications, such as empyema of the gall bladder or subphrenic abscess, can only be treated by drainage, aided by appropriate vaccine therapy. But should a fistulous opening have occurred into the bowel, expectant treatment is justifiable and, indeed, advisable. In any case of operation on a jaundiced person, calcium lactate in 15 gr. doses three times a day for three days before operation should be given to diminish the tendency to hæmorrhage.

5. **Cholecystitis.**—The medical treatment of this condition is essentially the same as for cholelithiasis, being summed up in the administration of salicylate and helmitol to disinfect the bile passages, calomel for the bowels, and free ingestion of alkaline mineral water, with hot applications over the gall bladder. Should the temperature become hectic and the leucocyte count continue to rise, drainage of the gall bladder by operation must not be delayed. It must be remembered that cholecystitis is one of the causes of fever without physical signs, and that, if the infection is due to B. coli, as it often is, there may be marked leucopenia.

6. **Treatment of Abscess of the Liver.**—(a) *Single or Tropical.*—This condition, which is a sequel of amœbic dysentery, calls for immediate operation, but subcutaneous injections of emetine, as advised by Leonard Rogers have an extraordinary effect in checking the hepatitis which precedes the abscess and will probably assist recovery after operation. The great liability of the abscess to secondary pyogenetic infections necessitates a rigid aseptic or antiseptic technique. If the abscess is already discharging through the lung, postural drainage should be tried. The patient hangs head downwards over a table, and in this position is made to cough and squeeze his chest. This may be repeated five or six times a day.

(b) *Multiple.*—Septic infection may reach the liver by: (i) the bile ducts, *suppurative cholangitis;* (ii) the hepatic artery, when it is part of an arterial pyæmia; and (iii) the portal vein, *portal pyæmia.* The treatment of the first variety is dealt with under the complications of gallstones, while the treatment of the second is that of the pyæmia, of which it is a comparatively minor part. Portal pyæmia, as I have shown elsewhere, is almost always due to a collection of pus under pressure within the portal zone. Appendicitis is the commonest precursor of such a collection, and was responsible for thirty-four, or just over 40 per cent., in a series of eighty-four cases I collected. Once established little can be done beyond symptomatic treatment. Blood-cultures may be sterile for a long time, as the organisms may be limited to the portal area, so that an autogenous vaccine often cannot be prepared. Surgical interference is only occasionally possible owing to the multiplicity of the abscesses, though successful cases have been recorded by Treves, S. West and Morton. Aspiration of the abscesses is not to be recommended, and fatal hæmorrhage into the peritoneal cavity has resulted from it.

7. **Treatment of Diseases of the Portal Vein.**—Suppurative pylephlebitis is merely a part of portal pyæmia. The commonest cause of pylethrombosis is cirrhosis of the liver, and was responsible for eleven out of twenty-five cases I collected (44 per cent.). It occasionally happens in new growth of the liver, and in the less virulently septic infections of the portal zone. Gastro-intestinal hæmorrhages or signs of intestinal obstruction are the leading symptoms in cases with acute onset, ascites in those coming on gradually. Little can be done in the way of treatment. The obstruction cannot be removed, and the only chance lies in supporting the patient until an adequate collateral circulation can be established. Even then, if the hepatic parenchyma be much involved, recovery is incomplete and temporary. Anything predisposing to gastro-intestinal catarrh must be avoided. Diarrhœa is a means of relieving the portal congestion, which we should not be too quick to check. If constipation occurs it should be remedied. Resection of the thrombosed portion of gut is a desperate remedy. On the ascites diuretics have little effect. Paracentesis should not be too long delayed, and, in spite of the loss of albuminous material, is usually well borne; the operation should, of course, not be performed too near the navel. Hæmatemesis should be treated just as in gastric ulcer. The Talma-Morrison operation for opening up fresh paths for collateral circulation is considered under *Cirrhosis.*

8. **Treatment of Cirrhoses of the Liver.**—(a) *Alcoholic or Multilobular Cirrhosis.*—The indications are: (i) to remove the cause, (ii) to relieve gastric catarrh, (iii) to relieve portal

congestion, and (iv) to assist collateral circulation. Chronic gastritis is a necessary preliminary to the production of fibrosis in the liver by alcohol. This accounts for the very variable action of alcohol in causing cirrhosis, and for the exceptional instances in which other poisons, such as mytilotoxin, appear to produce the same effect. It points also to careful oral antisepsis as an essential part of the treatment. But no treatment will be of any avail should the alcoholic habit be persisted in, and if self-control is so broken down that voluntary abstention is not likely to be maintained, initial treatment in an institution will be necessary. To diminish both the craving for alcohol and the gastric catarrh, I am accustomed to prescribe—

Tr. Capsici ♏ ii–v
Ammon. Brom. gr. x
Sodii Bicarb. gr. x
Spirit. Menth. Pip. ♏ x
Inf. Rhei ʒ ii
Inf. Gent. Co. ad ℥ i
t.d.s. ac.

If there is much morning retching a copious draught of water containing a drachm of bicarbonate of soda may help to clear off the mucus from the stomach, even if it is vomited.

To relieve portal congestion saline aperients should be given in the morning. An effervescent preparation like a Seidlitz powder may be the most grateful. An occasional dose of Pulv. Jalapæ Co. is sometimes useful, but fortunately the bowels often tend to be loose without drugs. The diet should be on the lines laid down for chronic gastritis (*q. v.*).

The occurrence of meteorism is suggestive of the onset of chronic peritonitis. A drachm of Ung. Hydrarg. Oleat. should then be rubbed into the abdominal wall every day, and 3 gr. capsules of benzo-naphthol with $\frac{1}{4}$ gr. of menthol every four hours may be given to relieve intestinal flatulence. If ascites supervenes and respiration becomes embarrassed there is no object in delaying tapping. Its appearance is always an unfavourable omen, and its speedy recurrence after tapping increases the gravity of the prognosis.

With a view of relieving ascites and assisting collateral circulation various operative measures have been advocated. Of these the Talma-Morrison operation is the best known; the upper surface of the liver and the lower surface of the diaphragm are scratched to promote adhesions, and the omentum is stitched to the abdominal wall. It must be pointed out that the operation is limited in scope, and cases must be carefully selected. For, in the first place, ascites is not a "back pressure" phenomenon in cirrhosis, but the result of chronic peritonitis, and, in the second, blood returning from the alimentary canal, which escapes passing through the liver by any short circuit, will contain substances which are not yet prepared for assimilation by the tissues and may be in some degree toxic. Thirdly, I have noticed at a post-mortem examination twelve months after operation that the omental adhesions were extraordinarily non-vascular. Again, advanced cases of cirrhosis notoriously stand operation badly, and if it is urged that early cases are more suitable, it may be replied that such are most suitable for medical treatment. Some years ago I saw a case of cirrhosis in a middle-aged woman with violent hæmatemesis. She then became drowsy, indeed almost comatose, for several days, while leucin and tyrosin crystals appeared in the urine. Yet she made a good recovery, and two years later was apparently in good health, having remained an abstainer. This could scarcely be called an early case, and had she been operated on, would naturally have been claimed as a brilliant success for that procedure. The immediate mortality of the operation is high, 37 per cent., but complete recovery is claimed for 31 per cent.

(b) *Hypertrophic or Biliary Cirrhosis.*—Probably various conditions have been thus designated, but the term should be restricted to the form described by Hanot. It is curious that cases seem to have been less common since examination of the blood became a routine procedure, and I am inclined to believe that the later stages of splenic anæmia (Banti's disease) were sometimes formerly taken for Hanot's cirrhosis. While the pathology is in such doubt treatment is necessarily unsatisfactory. On the view that it is caused by toxins reaching the liver by the general blood stream and leaving it by the bile ducts, systematic use of hepatic disinfectants, such as aspirin and urotropin, should be tried. Careful investigation may fail to reveal the nature of the toxin, but in one case of mine with marked infantilism, a positive Wassermann reaction was obtained after a small provocative injection of salvarsan. Otherwise the treatment can only be symptomatic and should be carried out on the lines laid down for other hepatic diseases.

(c) *Pericellular or Congenital Syphilitic Cirrhosis.*—The treatment is naturally that of syphilis. Salvarsan should not be used, however, as an initial treatment. It appears to cause such rapid disintegrative changes in the affected tissues that severe toxic symptoms may result. A prolonged course of mercury and iodide is safer, and in any case should precede the use of salvarsan.

(d) *Capsular Cirrhosis.*—This is usually associated with chronic peritonitis, and its treatment is that of the peritonitis.

9. Treatment of New Growth of the Liver.—The only innocent tumour of the liver is angeioma, which never produces any symptoms and is simply found at post-mortem examinations on patients dying of other conditions. Primary sarcoma is very rare and runs a very rapid course. Secondary sarcoma may be melanotic or lymphosarcoma. Primary carcinoma is rare, and then generally starts in the bile ducts. Though malignant disease of the liver in general is commoner in males, cancer starting in the gall bladder is commoner in females, suggesting chronic irritation by gall-stones as a factor in its production. If carcinoma of the liver is secondary the commonest situations for the primary growth are the rectum, stomach and uterus. Malignant disease of the pancreas seldom leads to large metastases in the liver.

The dyspepsia will require treatment on the lines of other forms of obstructive jaundice. One of the most troublesome symptoms is the intractable pruritus. Hot alkaline baths may be tried or some of the following preparations: a lotion of 1 dr. of creolin and 1 oz. of glycerine, made up with 10 oz. of water; an ointment of 20 gr. of camphor, 30 gr. of menthol and 1 oz. of vaseline; a dusting powder of $1\frac{1}{2}$ dr. of camphor, $\frac{1}{2}$ dr. of zinc oxide and 1 oz. of starch powder; a paint, or inunction, of $2\frac{1}{2}$ dr. of ichthyol, 3 dr. of absolute alcohol and ether to 2 oz. Other preparations which may help are Eichhoff's superfatted ichthyol-salicylic acid soap, prepared by Muelhens, of Cologne, or 10 per cent. of anæsthesine in olive oil. The difficulty about external applications for the pruritus is that the itching is *beneath* the skin. I have found thyreoid extract, in 5 gr. doses twice or thrice daily, the best remedy, as it diminishes the production of bile salts to the presence of which in the circulation the itching is due.

X-rays may be tried, though the most that can be expected is that they will check the rate of growth. Operation is usually definitely contra-indicated, though Keen has collected seventy-six cases of resection of tumours of the liver, sixty-three of which recovered. When more than one lump can be felt removal is impracticable. With the establishment of diagnostic tests for malignant disease of the liver, it is to be hoped that exploratory laparotomy, which is not well borne, will have to be resorted to less frequently.

W. L. B.

TREATMENT OF DISEASES OF THE EXCRETORY SYSTEM

FUNCTIONAL ALBUMINURIA

Functional albuminuria is a condition which is common in males between puberty and adolescence; it is much less common in females of the same age. Dukes found it in 16 per cent. of all the boys entering Rugby school. It is sometimes called "postural" or "orthostatic," to betoken the fact that the albumen appears only when urine is secreted in the upright position. Thus, it is absent from the urine passed on rising. It has sometimes been called "alimentary" but this is really a misnomer, for there is no evidence that the amount of albumen taken as food can influence the appearance of albumen in the urine. A possible exception to this is, that some constituent of raw eggs may, by exerting a toxic effect on the kidneys, excite a transient albuminuria. Indeed, considering how complete the breakdown of food proteins into amino acids is, it is difficult to see how excessive ingestion of protein could excite albuminuria.

Severe physical exercise will excite albuminuria in most healthy young adults. Thus, Collier found it present in every one of the Oxford crew of 1906, after rowing a course. Cold bathing may also induce transient albuminuria in such persons presumably by driving blood from the periphery into the splanchnic area. The albuminuria of exercise (to which the name "physiological albuminuria" may well be applied) need not be further considered here.

The subjects of functional albuminuria are usually anæmic, weedy youths with a dull, heavy aspect and a tendency to fainting. Their hearts are often irritable, and the condition vaguely diagnosed in lads as "weak heart" is frequently due to this. The blood-pressure is often very unstable, varying from hour to hour, and altering with posture in a way that the normal blood-pressure does not. There may be a difference of 40 mm. between the pressure in the upright and recumbent position. Examination of the urine may show, in addition to the albumen, a few hyaline casts and frequently calcium oxalate crystals.

The condition is unimportant, except that failure to recognise it may cause a boy to be labelled as a chronic nephritic, and his career seriously interfered with. In any case of albuminuria in a boy or a young man, the diagnosis of a kidney lesion should not be made unless casts other than hyaline are discovered, unless the tension of the pulse is definitely and permanently raised; and unless there are signs pointing to cardiac hypertrophy In the absence of such evidence, the urine passed

first thing on rising should be examined. If this is free from albumen, the condition is almost certainly functional. Then 15 gr. of calcium lactate should be given three times a day for three days. At the end of this time the urine should be examined again. In functional conditions, it is probable that the drug will have checked the albuminuria. If so, no further anxiety need be felt. If the patient has been working hard (and the condition is very apt to occur under the strain of competitive examinations), he should have a holiday, and be told not to worry about his health. A tepid bath with cold sponging down the spine, followed by vigorous towelling, generally suits such cases. As to drugs, calcium lactate is usually prescribed on Sir Almroth Wright's view that the condition is due to diminished viscosity of the blood. This contention is by no means generally accepted, however. I have sometimes given digitalis in small doses, such as 5 min. of the tincture three times a day, to try and brace up the lax state of the vasomotor system. Possibly pituitary extract, with its power of increasing normal muscular response, may prove to be of more service. A good general tonic, such as strychnine, is generally indicated with iron if there be any anæmia. The condition soon rectifies itself when adolescence has passed, and any case of albuminuria in a patient approaching thirty should be regarded as probably organic, and not merely functional. In conclusion, the recognition of this comparatively harmless condition is of far more importance than its treatment.

W. L. B.

ACUTE NEPHRITIS

The dictum that "in acute affections we concentrate our attention on the diseased organ, whilst in chronic cases we keep the general condition of the patient more in view" applies particularly to the treatment of nephritis.

In acute nephritis, the dangers of overloading the inflamed kidney with nitrogenous substances is apt to be disregarded; whilst, in chronic nephritis, the restriction of diet is apt to be too severe. Our aim in acute nephritis must be to remove, if possible, the microbic or toxic cause at work and to ensure such physiological rest for the kidney as is practicable; to promote elimination of nitrogenous and saline waste by other channels; to treat complications as they may arise and to correct the resulting anæmia. In this way much may be done to steer the patient towards recovery, although we can do little to control the course of the inflammatory process.

The patient is naturally kept recumbent in bed. Horder advises frequently moving him from side to side and occasionally on to the chest. This simple method of combating with effects of gravity should be more extensively employed than it is. To guard against chills and to encourage free action of the skin, he should be clad in a flannel nightgown and placed between blankets. The room should be warm and well ventilated. If suppression of urine threatens, dry cups may be applied over the loins.

1. *Diet.*—Nitrogen retention is a prominent feature and a source of danger in acute nephritis, so that the free administration of milk usually recommended is open to objection, since cow's milk contains 4 per cent. of protein, which equals 0·56 per cent. nitrogen. It will do little harm to deprive the patient of nitrogen for a time, and Von Noorden advises restriction of the diet at first to simply fruit-juice, water and sugar. Where there is no nausea, I have allowed toffee, which, being composed of butter and sugar, throws no work on the kidney; it is generally appreciated by children and allays hunger. Barley-water, with a little milk added, may also be given, and as the patient improves the proportion of milk may be increased. It is quite unnecessary to give anything else for a few days, and the relatives' fear of starvation must be allayed by explaining the rationale of the treatment. It is well to avoid salt in any form, as it is often badly excreted and its retention increases œdema by raising the osmotic pressure of the tissues.

Flushing out the kidneys is usually advised, and to this end the patient is directed to drink large amounts of water, but the inflamed kidney will not excrete water readily, so that attempts at flushing it out really only increase the œdema. The total amount of fluid allowed in the day should not exceed three pints for an adult or one and a half pints for a child of twelve. It is true that after some days there may be a sudden diuresis; this, however, is not the result of treatment, but the first and surest sign of convalescence. It may be termed a critical diuresis, and, after its occurrence, the quantity of water and milk ingested may be considerably increased with advantage; then bread and butter, potatoes and cream may be allowed. Beef-tea, broths, and meat-juices are all to be condemned as imposing work on the kidney with very little corresponding nutritive advantage.

A drink prepared by adding a pint of boiling water to a drachm of acid tartrate of potash, half a fresh lemon and some sugar, stirred occasionally until cold and then strained, may be allowed throughout in moderate quantities. The tartrate and citric acid become bicarbonates in the blood, and, by making the urine less acid, may render it less irritating; moreover, any

diuretic effect they may have is at the expense of the œdema of the tissues.

2. *Elimination by Other Channels.*—Of these the simplest and best method is purgation. A drachm of Pulv. Jalapæ Co., followed by a drachm each of sulphate of magnesia and sulphate of soda in as concentrated a solution as possible, should be given at the outset and repeated as occasion arises. Diaphoresis is not nearly so satisfactory and certainly should not be carried to excess lest the heart may become depressed. It is usually sufficient to sponge the patient well with hot water, followed by friction with warm, dry towels. The warm room, the blankets and the flannel nightgown also tend to produce perspiration. In my opinion, more drastic measures are seldom advisable in acute nephritis, except possibly in impending uræmia (*q.v.*).

3. *Drugs.*—No stimulating diuretics should be given at all. Saline diuretics such as potassium citrate probably do no harm and, as explained above, help to render the urine less irritating. The following prescription may be useful and is mildly diaphoretic—

Pot. Cit. gr. xv
Liq. Ammon. Acetatis ʒ i
Sp. Æth. Nitr. ℳ xv
Aq. Camph. ad ℥ i
Sextis.

The addition of 5 min. of tincture of strophanthus and 3 min. of Liq. Strych. is advisable if the heart's action becomes weak.

4. *After-Treatment.*—Bed is, of course, imperative until blood has disappeared from the urine, and is advisable until albuminuria has ceased altogether. This may be impossible, since acute nephritis may have sown the seeds of chronic nephritis, but there is, nevertheless, a great advantage in prolonging the rest as much as possible.

Fish and eggs, and later vegetables, may be added to the diet as the albuminuria diminishes, but meat and meat extracts should not be taken for a long time.

For the resulting anæmia few things are better than the Liq. Ferri Acetatis, of which 15 min. may be given with 1 dr. of Liq. Ammon. Acetatis in camphor water three times a day.

It is important that all possible precautions should be taken against chills, and the loins may be protected by the wearing of a cholera belt.

W. L. B.

CHRONIC DIFFUSE NEPHRITIS

It would be generally agreed that the orthodox, conventional treatment of chronic nephritis includes the following principles—

1. Severe restriction of protein intake with exclusion of food rich in albumen, such as eggs. In severe cases absolute restriction to simple milk diet.

2. The estimation of the amount of urea in the urine is to be taken as a guide to the capacity of the kidney.

3. The kidney is stimulated to increased excretion by the use of diuretics.

4. Elimination by the skin is promoted by various diaphoretic measures.

I venture to assert that each of these principles contains, and, indeed, is based upon, a fundamental fallacy.

In Bright's disease we have probably been inclined to lay too much stress upon the albuminuria. In the chronic parenchymatous form, no doubt the drain on the albuminous constituents may become serious and a secondary anæmia may result. But such high degrees of albuminuria are uncommon, and we are beginning to realise that this one symptom has unduly dominated our conceptions of the disease. Von Noorden thinks that any wasting is just as much explained by the monotonous diet as by the loss of albumen.

Chronic Parenchymatous and Chronic Diffuse Nephritis.—Chronic nephritis is often sub-divided into parenchymatous, interstitial and mixed. The interstitial form, granular kidney, presents so many points of distinction that it will be well to deal with it separately. The present tendency is to regard all cases of chronic nephritis involving the parenchyma of the organ as diffuse from the first, though, naturally, the interstitial changes take longer to manifest themselves. It is certain that, when parenchymatous nephritis has existed for any length of time, there will be interstitial change as well. In treatment no special distinction has to be drawn between chronic parenchymatous nephritis and chronic diffuse nephritis. In the latter it is not likely that œdema will be a marked feature calling for special attention. As a prophylactic measure it is essential that the after-treatment of all cases of acute nephritis shall be thorough and prolonged. It is seldom possible to treat the cause of chronic nephritis; only in syphilitic cases and in those of possibly malarial origin can this be done. Confinement to bed is only advisable during exacerbations, when dropsy is extreme, or when uræmia is threatening.

1. *Diet.*—The tendency in the past has been to restrict the protein diet in chronic nephritis too much, probably owing to false analogies with glycosuria, whereas there are certain essential differences; thus, a certain minimum amount of protein is an absolute necessity, while sugar can be replaced to a considerable extent by other things in a diet. Again, glycosuria is usually preceded by hyperglycæmia, while there

is no excess of albumen in the blood before albuminuria occurs. On the contrary, in nephritis the damaged kidney allows normal proteins to escape. Moreover, the proteins of the food are broken down into small molecules of amino acids before absorption. The evidence that albumen can be absorbed as such and is able to "run through" the body will not bear investigation. It is difficult, therefore, to believe, on theoretical grounds, that the albuminuria of nephritis can be directly influenced by the amount of albumen in the diet. I have tested the point practically in a good number of cases of chronic nephritis, and have found that the addition of three eggs to the daily diet has had no effect on the albuminuria.

This is not to say, of course, that unlimited protein is good for the nephritic. We know now that the physiological amount of protein necessary in the day is less than was formerly thought. Chittenden has clearly shown that nutrition can be maintained on 50 to 60 gm. of protein a day. We may say, then, that the minimum protein allowance for a chronic nephritic is 50 to 60 gm. plus the amount of protein which he is losing in the urine. In a case of ordinary severity this will be about 6 gm. a day, which is the same amount of protein as that contained in one egg. Von Noorden has shown that the ordinary chronic nephritic can excrete his nitrogen satisfactorily so long as he does not take more than 94 gm. of protein in the day. Above this amount, elimination becomes irregular and uncertain. This may, therefore, be regarded as the practical maximum, while 50 gm. of protein may be regarded as the theoretical minimum. There is not, then, a wide difference between the theoretical and practical conclusion. We should naturally avoid meat extracts and cellular organs, such as liver, kidney and sweetbread, because they contain a large amount of purins, which are useless for nutrition and necessitate excretion by the kidney; according to Von Noorden, the damaged kidney excretes uric acid with difficulty. To give such substances is contrary to the principles of physiological rest, but we must equally avoid such restriction of the diet as to lead to failure of appetite and consequent wasting while incapable of diminishing the albuminuria. We can safely permit a much greater variety of diet than is usually allowed; for instance, I believe from my analyses that eggs and dishes made from eggs certainly may be allowed. The eggs should not be taken raw, because raw eggs contain certain indeterminate substances which may have an irritant effect upon the kidney. The distinction drawn between red and white meat is fallacious. Red meat is assumed to have a more injurious action, presumably because it is supposed to contain more purin bodies, but the reddest meat, such as rump-steak, contains far less purins and other extractives than a white meat such as sweetbread. Again, mutton contains less purin than chicken. The practical conclusion is that small quantities of fish, mutton and ordinary beef may be allowed, while soups, broths, internal organs and rump-steak should be forbidden. But within these limits a wide variety of choice may be permitted. It is undesirable to restrict chronic nephritics to milk, which is too dilute a form of food for them and may increase œdema. Salt should not be allowed, since it is badly eliminated in many cases of nephritis and, accumulating in the tissues, increases œdema by raising their osmotic pressure. Indeed, as Bryant found, even a man with a healthy heart and kidneys may develop œdema as a result of taking excess of salt. The substitution of fresh butter and lemon-juice will usually satisfy the patient.

In following this plan, we shall avoid adding to the miseries of sufferers with an incurable disease by enforcing unnecessary restriction. If it be desired to guard against the dangers of possible nitrogen retention, Ernberg's plan may be followed of interposing periods of a week or a fortnight during which a diet poor in protein is taken. But prolonged nitrogen starvation is as bad for the nephritic as for any one else.

Generally speaking, alcohol is inadvisable in any form, and should never be ordered to those unaccustomed to it. In the case of patients in the habit of taking it regularly, deprivation may interfere with their appetite, in which case a little well-diluted whisky is probably as innocuous as any form of alcohol can be. But the strictest moderation must be enjoined.

Tea and coffee are usually forbidden because of the methyl-purins they contain. Although this is theoretically sound, many patients find this restriction very onerous, and, if there is no sign of exacerbation, I have allowed moderate quantities of China tea (which contains only about half as much purins as Ceylon tea) made weak and with plenty of milk, or made in the Russian manner with a slice of lemon.

2. *Determination of Urea Output.*—Within wide limits, the amount of urea excreted depends on the amount of protein eaten and on very little else, since the greater part of the urea comes direct from the food. It is incorrect to suppose that the amount of urea excreted is any real guide to the severity of the case or provides any indication as to the degree of restriction necessary in the diet. Of course a patient on the diet ordinarily given in nephritis passes less urea than a normal individual, since he is given a diet poor in protein. The more the diet is restricted, the lower will be the output of urea. The only help which can be got from

estimating urea is in conjunction with the total output of nitrogen as determined by Kjeldahl's method. Then it can be seen whether a proper percentage of the nitrogen is converted into urea. This should not be less than 80 per cent. of the total. But simple estimations of urea without determining the protein intake and the total nitrogen output are useless, misleading and should be abandoned.

3. *Diuretics.*—Flushing out the kidney is generally regarded as a good line of treatment in chronic nephritis, but before employing it we should consider what method of diuresis we mean to use, how far such methods are desirable in an individual case, and how far they will achieve the end desired. Routine and indiscriminate "flushing out" is to be condemned.

The following are possible methods of producing diuresis: (*a*) by vaso-dilatation in the kidney, as by caffein, theobromine, theocin sodium-acetate or diuretin. These probably act as direct stimulants to the renal epithelium, the vascular change being secondary. (*b*) By vaso-constriction elsewhere, in consequence of which the blood pressure is raised and more blood is forced through the kidney. (*c*) Increase in the quantity of the circulating fluid: (i) by absorption of water from the intestines, as by giving the patient large quantities of fluid to drink; (ii) by increasing the osmotic pressure of the blood. The saline diuretics—citrates, acetates, etc.—act in this way, drawing water from the tissues into the blood stream.

How far are these methods desirable in the treatment of nephritis? The first group are stimulants, and it is doubtful policy to stimulate a damaged structure. I have seen bad results follow the use of caffein, theobromine and diuretin. It is chiefly in chronic parenchymatous nephritis that they are employed and there is a danger that they will cause a return of acute symptoms, such as hæmaturia. I have gradually come to the conclusion that this group of drugs is unsuitable for nephritis and that they should be restricted to those cases where diuresis is required and the kidneys are not organically diseased. The same applies to juniper and scoparium. An exception may be made in the case of theocin sodium acetate which in doses of 2 gr. twice a day may produce a distinct improvement. It appears to render the kidney more permeable.

As to the second method of diuresis, since the blood pressure is generally raised in chronic nephritis, it seems unnecessary to raise it further. Digitalis is the drug usually employed for this purpose, but modern research has tended to overthrow its claim to raise blood pressure in human beings, and its diuretic action is now thought to be purely secondary to its cardiac action. If so, it should only be used as a diuretic in cases where the heart is failing. Even here I have seen it fail when the blood pressure was already high and the failure of urinary secretion was due to a secondary back pressure.

Again, in chronic nephritis there is a defective adjustment of the kidneys to varying water supply. Von Noorden has shown that, whereas a normal individual with an average hourly diuresis of 52 c.c. excreted an average of 723 c.c. for three hours after drinking 1800 c.c. of Salvator water, the nephritic hardly showed any response of this kind. As in acute nephritis, the drinking of large amounts of fluid may therefore merely increase the œdema.

Yet it is certainly desirable to achieve diuresis in chronic parenchymatous nephritis if possible. The attempt to increase the urinary flow by increasing the osmosis into the blood is less open to objection, for, as explained under *Acute Nephritis*, since the extra water is drawn from the tissues, it will tend to diminish and will not increase the œdema. As in the later stages of acute nephritis, I believe the best diuretic is a combination of 15 min. of Liquor Ferri Acetatis with 1 dr. of Liquor Ammonii Acetatis. This has the advantage of helping to correct the secondary anæmia.

If this has not the desired effect, the reaction to drinking a pint of water may be determined, but, unless it causes a definite increase in the amount of urine, it is no good persisting with the flushing-out method. In the presence of œdema it is not likely to be successful. The reaction to 2 gr. of theocin sodium-acetate twice a day may also be determined, but it is well also to test the urine daily with tincture of guaiacum and ozonic ether for blood, and the drug must be discontinued at once if the slightest trace is found. In any case, it should only be used for a limited time, and only if necessary in view of the continued falling off in the amount of urine.

4. *Diaphoretics.*—The arguments for and against diaphoretic measures in the treatment of nephritis will be found under the treatment of Uræmia. Diaphoretic drugs seem to me to be particularly unsuitable in the routine treatment of chronic parenchymatous nephritis, as a moist perspiring skin would render the patient more liable to chills, always an outstanding danger in this disease. A course of hot-air baths if there is retention of salt and increasing œdema may sometimes be helpful. I have seen this produce diuresis, which can only be explained as due to elimination of salt and consequent lowering of the retentive power of the tissues for water.

5. *Purgation.*—Free elimination by the bowel is here, as in other forms of nephritis, a prime requisite.

The use of mercurials for this purpose is not free from risk, as the sufferer from chronic nephritis is specially liable to stomatitis. Few things are better to start a free action of the bowels than Pulv. Jalapæ Co., of which 1 to 2 dr. may be given to an adult. When there is much dropsy, Matthew Hay's method of giving 6 dr. to 1 oz. of magnesium sulphate in 1 oz. of water before breakfast may be tried. In this concentrated form it is apt to excite nausea; if not, it will be found very effective in producing a watery evacuation.

6. *Paracentesis.*—Removal of the ascitic fluid by Southey's tubes is seldom practised now, though simple incisions are sometimes made. The wounds are very likely to suppurate and the fluid will re-accumulate as long as the conditions remain unfavourable. Ewart recommends drainage of the fluid into the legs by adopting the upright posture; the fluid, which presumably is loaded with toxic substances, is thus removed from the vital organs.

7. *Climate* may prove a valuable help in the treatment of chronic nephritis. Egypt generally suits these patients particularly well. Algiers is also quite suitable. The wind and the more violent fluctuations of temperature on the Riviera render it much less advisable. In this country Ventnor, or anywhere on the south coast from Bournemouth westward, is the most suitable climate that can be obtained.

It may fairly be objected that I have attempted to destroy the basis for treatment without being able to put anything in its place. To a certain extent this is true. The kidney, once damaged by chronic nephritis, cannot recover, and the only thing which can be done is to attune the mode of life to a low key, subjecting the patient to as little strain as possible. He must be warmly clad and the kidneys protected from fluctuations of temperature as far as possible. He may have a considerable variety of food provided that the intake of protein does not fall below 60 or rise above 90 gm. in the day, and provided that he takes very little purins and salt. In constructing the dietary it will be convenient to remember that a pint of milk, one egg, a quarter of a pound of fish, and two ounces of meat contain altogether 72 gm. of protein. Allowing for the protein in bread and vegetables it will be seen that the amount of nitrogen in this diet errs rather on the side of liberality. It will, however, serve as a rough guide. He can be helped by saline diuretics and unirritating preparations of iron. He will do all the better if his medical man realises that many of the methods recommended in the treatment of this disease are impotent where not actually harmful.

W. L. B

CHRONIC INTERSTITIAL NEPHRITIS

The causes of chronic interstitial nephritis or granular kidney are essentially the same as those of arterio-sclerosis; in some cases the stress falls upon the large arteries and the kidneys suffer secondarily, in others the kidneys suffer first, necessitating a rise of blood pressure to effect due circulation through them, with consequent detriment to the arteries. Treatment must be directed in the first instance to removing the cause where possible; thus gout, alcohol, lead and syphilis are the special artery destroyers. But there are also poisons absorbed from the alimentary tract, such as the diamines formed from the putrefaction of proteins, which have been shown to have a definitely pressor effect, and must in time damage both arteries and kidneys.

In some cases no cause can be found, but there is a family tendency to the condition, as if, in Sir William Osler's phrase, "inferior rubber had been used in the tubing." Such patients may have lived exemplary, frugal, self-denying lives; not infrequently they have been the subjects of migraine in earlier days. I have seen some marked examples of this type in women. There is not so much to be done in the way of treatment here, for the mode of life calls for little alteration, and they do not stand restriction of diet well. But in the main, granular kidney is a typical disease of modern civilisation induced by rush and strain, over-eating and over-drinking, burning the candle at both ends.

General Prophylactic Measures.—The timely discovery of a trace of albumen and casts in the urine should act as a danger signal, enabling the brake to be applied before disaster occurs. But it is still more to the advantage of the patient if the condition is recognised while he is still in the stage of merely raised arterial tension, before organic changes have taken place. It can hardly be doubted that such a functional stage does occur, probably in every case. For its recognition we must rely on the sphygmomanometer in middle-aged patients who complain of shortness of breath on slight exertion, giddiness on rising quickly from a chair, frequent headaches, bilious attacks, epistaxis, difficulty in mental concentration, irritability or insomnia. For a patient with granular kidney complains of these effects of raised arterial tension; the large amount of limpid urine is usually a matter for pride rather than anxiety with him, and lumbar pain, despite the advertising vendor of patent remedies, is almost unknown.

In the full-blooded type of patient "full of coarse strength and butcher's meat" much may be done by regulating the diet and altering

the mode of life. Late hours, evening meetings in stuffy rooms, especially when accompanied by heated political discussions are to be condemned. In few conditions are both the dish of herbs and contentment more essential, or the stalled ox and strife more injurious.

Diet.—The bulk and number of the meals should be reduced; roasted meat must be partaken of sparingly, while soups, gravies and internal organs should be avoided altogether. On the other hand, fruits, green vegetables, farinaceous and non-nitrogenous foods may be taken freely. The salt added at table should be stopped, and in severe cases a salt free diet may be advisable for a time. If the pressure shows a continued tendency to rise, a few days' rest in bed on a milk diet is advisable. Soured milk can only be expected to be of service where there is definite evidence of intestinal intoxication. Coffee, tea and tobacco should be limited, and in certain cases excluded. Thus tobacco should be forbidden if it causes cardiac distress or pain; in my experience this is most likely to occur if mixtures containing Cavendish or Latakia are smoked. Alcohol is usually bad for such patients, except where the heart is weak and the appetite poor; then a small quantity may be allowed with food, but drinks between meals must become things of the past.

Baths may be a valuable adjunct to treatment. A cold bath is inadvisable, but a warm bath either at night or on rising will be beneficial. In the latter instance the warmth may be gradually reduced by running in some cold water. The advisability of Nauheim baths (the materials for which can now be readily obtained) is not so certain. It is not that their efficacy in lowering pressure is doubtful; the objection is that they do so by direct vaso-dilatation. They may be followed by rather alarming faintness. The Turkish bath may suit some cases very well as long as there is no cardiac distress in the hot room and a sufficient time is allowed for cooling and rest. Plombières douches are recommended where there is suspicion of intestinal intoxication. An annual course of balneological treatment is often very useful; the regulation of the life, freedom from worry and the change of surroundings are probably of more importance than the chemical ingredients of the water. The kidneys will respond to increased ingestion of fluids readily enough, but there is no proof that the flushing-out treatment is beneficial even here. Von Noorden considers that moderate restriction of fluids, say to 1½ litres or rather more than 2½ pints, does not diminish nitrogenous excretion and spares the heart.

Climatic Treatment is of value as in other forms of chronic nephritis (*q. v.*).

Aperients.—It is of the greatest importance that the bowels should be kept freely open, to eliminate both the toxins from the body and the pressor diamines formed in the bowel. Sulphates are specially indicated for this purpose, since they are used by the body to combine with putrefactive substances and thus render them innocuous. As sodium sulphate is more readily absorbed into the circulation than the more aperient magnesium sulphate, preference should be given to the former, since this combination is effected in the liver. A weekly dose of calomel or mercury pill may also help, but as in other forms of nephritis, there is risk of mercurialism if they are given more frequently.

Exercise in the open air, without strain, and not carried to the point of affecting the pulse or respiration is a great help in these early cases. If modern conditions of life are largely responsible for granular kidney, they have also evolved a most useful prophylactic measure by popularising golf, the best form of exercise for those liable to these degenerative changes. But rest after meals should not be curtailed. In many cases the response to such simple, physiological methods of treatment has been remarkably good, enabling patients to continue to lead a useful and active life.

Depressor Remedies.—The great objection to lowering arterial tension by drugs is that we do not know what is the correct pressure for any particular degree of interstitial nephritis. Certainly some elevation of pressure is necessary, as it is essentially a conservative process which should not be directly antagonised by vaso-dilators. Like a rise of temperature in an infection, the rise of pressure in granular kidney is a symptom. In all pathological attempts at repair, however, the body may overshoot the mark, and it may then become as imperative to lower the pressure as to treat hyperpyrexia. In such a case those drugs should be chosen which have a slow and prolonged action. The fall of pressure produced by amyl nitrite is too brief to be registered by the manometer. Nitro-glycerine only lowers pressure for forty minutes. Erythrol tetranitrate in ½ gr. doses, on the other hand, will produce a fall lasting six hours. The chief objection to its use is its tendency to cause severe headache in some patients. Mannitol also produces a prolonged effect. Oliver recommends the tabloids Sodii Nitrit. Co. prepared for him by Burroughs and Wellcome which have the following composition—

Sodii Nitrit. gr. ss
Erythrol Tetranitrit. gr. ¼
Mannitol Nitrit. gr. ¼
Ammon. Hippurate gr. i.

One of these tabloids may be taken twice or thrice a day. If given for lengthy periods they

should be omitted for a few days or a week in each month.

Potassium iodide falls into a different category. It is doubtful whether it has any special action on the calibre of the blood-vessels. But it has a distinct effect on the elimination of poisons such as lead, mercury and the toxin of syphilis. The undoubted benefit from its use in some cases of granular kidney with high pressure is probably due to its eliminative action on the various and vaguer toxins here concerned, so that it is not merely attacking a symptom but may be striking at the root of the mischief.

Guipsine has also been recommended in such cases and may be administered in pills containing three quarters of a grain. As, however, it acts through the vasomotor system, it seems to me to be open to the same objections as the nitrites.

Venesection finds warm advocates, but it is to be looked upon rather as an aid in an emergency arising from high pressure than as suitable for general treatment. But such success as the old-fashioned routine "blood letting" achieved was presumably in cases of this nature. And after all it is only imitating nature's way of dealing with them by epistaxis.

Patients who are inclined to be nervous about their condition should not be told the reading of the manometer, and they should never read the index themselves, as this may easily send the pressure up 10 mm. But if they are told that there is an improvement, the pressure will probably fall at once, showing the effect of mental agitation. Indeed the introduction of the sphygmomanometer has produced a new form of neurosis, in which the patient is constantly thinking about his pressure, and for this it is to be feared the medical profession is responsible.

The albuminuria of granular kidney is slight in amount and unimportant in its effect. It calls for no treatment.

Treatment of Complications.—In so far as the change in the kidneys has occurred in chronic interstitial nephritis it is permanent, and we can only resist the encroachments of the disease step by step with the aid of the physiological principles already laid down. But special symptoms may arise from time to time, some of which will call for treatment.

Dyspnœa is due to one of two things, uræmic "asthma" or failing heart. In the former case the patient will probably be drowsy and the gums may be spongy while the pulse will probably remain regular. There is likely to be sweating and the volume of the urine will be diminished. It must be treated as described under uræmia, by free purgation, diminished nitrogen intake, large doses of sodium bicarbonate and perhaps venesection. The use of stimulating diuretics is less open to objection in this form of nephritis, and the following mixture may be ordered every four hours—

Diuretin gr. x
Potass. Tart. gr. xx
Spirit. Juniperi ♏. xxx
Inf. Scoparii ad ℥ i.

Or 2 gr. of theocin sodium-acetate may be given every six hours.

If the dyspnœa is due to the heart failing behind the excessive pressure there will probably be an irregular pulse, a more marked reduction in the secretion of urine and œdema of the legs. This last symptom only occurs in granular kidney when the heart begins to fail. Complete rest is indicated, and 5 min. of Tr. Strophanthus with 5 gr. of potassium iodide should be given every four hours. If this is not enough, oxygen should be inhaled to spare the work of the right heart, and venesection may be tried. Nitrites given on the plan already described may help to tide over the difficulty. Although morphia is rightly considered risky in diseases of the kidney, there is no doubt that it may afford great relief in cardiac distress and may justifiably be given a cautious trial. But cardiac symptoms show an important downward step in a case of granular kidney. Henceforward we are on the horns of a dilemma; if the pressure is allowed to become too high there is danger either of cerebral hæmorrhage or cardiac failure, while if it is lowered too much the patient feels miserable and depressed, and the urinary excretion becomes inadequate, so that toxins accumulate in the tissues.

Epistaxis is a safety-valve which should not be checked too soon, *hœmaturia* is of a similar character and calls for no special treatment. *Retinitis* cannot be treated. The treatment of a complicating *pleurisy* or *pericarditis* must be on the ordinary lines. *Digestive disorders* are due to a mild chronic uræmia and should be treated by restricting the nitrogen in the diet and by free purgation. *Insomnia* may yield to diffusible stimulants such as 20 min. each of Sp. Æth. Nitrosi, Sp. Æth. Co. and Sp. Ammon. Aromat. well diluted. Another remedy is 20 gr. each of bromide and chloral-amide. S. West considers Cannabis Indica the best hypnotic in this disease. But it may be necessary to resort to morphia to break the sequence of restless nights which are wearing the patient out. W. L. B.

URÆMIA

Broadly speaking, the most acute or fulminating forms of uræmia will manifest nervous

symptoms, while the subacute will display respiratory disturbances, and chronic uræmia will lead to gastro-intestinal troubles. This distinction is more apparent than real, for the respiratory and gastric symptoms are central in origin, being due to the action of a toxin on the medulla. Diarrhœa, on the other hand, is often due to "albuminuric" ulceration of the intestines, and, therefore, in my opinion, is better not regarded as a manifestation of uræmia. Again, in both the respiratory and gastric types, purely nervous symptoms will probably occur as the case gets worse. From the point of view of treatment, the important thing is to recognise the uræmic character of such manifestations.

Uræmia may occur either in the course of acute or chronic nephritis. A child with previously healthy kidneys may develop uræmia within forty-eight hours of the onset of scarlatinal nephritis, and a man may become uræmic who has been known to be the subject of granular kidney for years.

The treatment of uræmia is unsatisfactory, as the underlying cause is usually an incurable and progressive lesion. Indeed, only in acute nephritis can we expect to do more than stave off the fatal issue for a short time. When uræmia depends on an acute congestive nephritis the engorgement of the kidneys may be relieved by dry cupping of the loins. Four cups should be applied. For the relief of vomiting I have had most success with the administration of 1 min. of Tr. Iodi and ½ min. of carbolic acid in 1 dr. of water every quarter of an hour for three or four hours.

Apart from this, the primary indication in the treatment of uræmia is the rapid elimination of the accumulating toxins in every possible way.

1. **Elimination by the Bowel.**—Of all the routes available, the bowel is the simplest and one of the most effective to bring into action. For this reason we should never be in a hurry to check the diarrhœa which may be present, as it is nature's effort to eliminate toxins. The irritating effect of these toxins is probably responsible for the ulceration which may be revealed at the post-mortem examination. Von Noorden has shown that 8 gm. of nitrogen can be eliminated by the bowel, while not more than 3 gm. can be got rid of by the skin. Such drastic means as croton oil, elaterium and gamboge are seldom to be recommended; they are too irritant for an already irritated intestine. Five gr. of calomel followed by ½ oz. of magnesium sulphate, should be tried, or 1 dr. of Pulv. Jalapæ Co. In milder cases of chronic uræmia the compound colocynth pill every other night may be sufficient. If not, 1 oz. of Mist. Sennæ Co. should be given without delay.

2. **Elimination by the Kidney.**—The limitations of diuretics in nephritis apply with even greater force to uræmia, for the condition is a manifestation of the failure of the kidney to do its work. Very little can be expected, therefore, from diuretics in uræmia. In parenchymatous nephritis the stimulating diuretics, such as caffeine, are liable to do harm by irritation of the kidney. (For discussion of the action of diuretics in nephritis, see article on *Chronic Nephritis.*)

3. **Elimination by the Skin.**—This method of treatment is open to the following objections: (1) Very little nitrogen can be got rid of through the skin compared with the amount that can be eliminated by the bowel. (2) Physiological rest for the kidney is not secured by giving it a highly concentrated urine to deal with, for defective adjustment of the kidney to varying concentration of the urine is a prominent feature of nephritis. (3) Diaphoresis is an exhausting process and depressing to the heart. (4) The withdrawal of so much fluid without a corresponding removal of organic solids must increase the concentration of the toxins in the circulation.

If, therefore, it is decided to employ diaphoretic measures in uræmia, it should be, after fully weighing these objections, as applied to the particular case. It has been urged in support of this method of treatment that, after a hot-air bath, the patient may be actually covered over with small crystals. These crystals, however, in the main do not consist of urea, but of sodium chloride. And here we have the clue to the kind of case in which diaphoresis may be of service, namely, that in which there is a defect in the elimination of sodium chloride with consequent œdema. For the retained salt increases the osmotic pressure of the tissues, and this tends to increase œdema and to diminish excretion. The elimination of salt by the skin may, therefore, be of indirect service by breaking a vicious circle. The vapour bath or hot pack may also be used, but they are more trying to the heart than the hot-air bath. None of these procedures should be continued for more than a quarter of an hour after sweating has begun, a careful watch must be kept on the pulse, and the bath or pack stopped at once if there is any sign of collapse; stimulants should be at hand. Pilocarpin occasionally produces a great improvement, but is a dangerous method of bringing about diaphoresis. It is profoundly atonic in its effect on the heart. Moreover, as it causes outpouring of other secretions besides that of sweat, a drowsy patient may be drowned in his own pulmonary and bronchial exudate. It is given as the nitrate in doses of $\frac{1}{16}$ gr. hypodermically, or $\frac{1}{8}$ gr. by the mouth. It should not be repeated within four hours.

After diaphoresis, the temperature may fall dangerously low in spite of hot bottles and blankets. The temporary improvement which is produced sometimes by this treatment may be, in my opinion, purchased too dearly at the expense of the subsequent exhaustion.

4. Elimination by Bleeding.—A spontaneous epistaxis has been noticed to avert an attack of uræmia, and there can be little doubt that venesection is the most rapid method of removing some of the toxins. This can be combined advantageously with infusion with normal salt solution. In this way a larger amount of blood can be abstracted and the toxins diluted. As the vascular tension is usually high the volume of infused fluid should be less than that of the blood removed. Thus 30 oz. of blood can be removed and 20 oz. of saline infused. If the blood pressure remains high after venesection, say over 170 mm., vaso-dilators, such as nitroglycerin, $\frac{1}{100}$ gr., may be given every four hours. Removal of cerebro-spinal fluid by lumbar puncture is recommended by some authorities, and is a rational procedure, since the toxins must presumably be present there in considerable amount.

Inhalations of oxygen have been recommended, but any benefit derived is probably due to its cardiac effect. As Lewis and Barcroft have shown that uræmic asthma is due to an acidosis large doses of alkalis should be given as in diabetic air-hunger. Inhalations of chloroform are probably the best treatment for uræmic convulsions. Osler strongly recommends morphine, considering it indispensable for the restlessness and delirium. I have certainly known it to do good in the extreme restlessness and dyspnœa of chronic uræmia in consecutive nephritis, but I am inclined to agree with Burney Yeo that, if it be freely used for this purpose, the restlessness of uræmia may be relieved by the repose of death.

W. L. B.

MOVABLE KIDNEY

Before discussing the treatment of this condition, it is necessary to define exactly what one means by the term "movable kidney." To many the term implies a kidney the lower pole of which can be palpated during inspiration. This is certainly an incorrect view to hold, for careful examination reveals the fact that the lower pole of the kidney can be felt in a very large number of spare individuals under these circumstances. Abnormal mobility may be said to exist in a kidney which has definitely prolapsed so that half to three-quarters or more of its surface can be palpated, or in one which has undergone rotation around a horizontal axis, without undergoing any prolapse. Such a kidney will not be palpable at all, but must be included in the classification, as it is in this form that the most acute symptoms, those known by the name of Dietl's crises, occur. A large majority of the patients who develop movable kidney are women. In many cases the kidney produces no symptoms at all, and is only discovered during the routine examination of the patient. In these cases the best treatment is to say nothing about the kidney to the patient, but to make a note of its existence, and possibly to inform the friends or relatives of the patient of the condition, at the same time pointing out that the kidney is giving rise to no trouble. I cannot too strongly protest against the opinion which has been advanced in certain quarters that almost any conceivable disease, from insanity to appendicitis, may be caused by undue renal mobility.

Treatment is only demanded in cases of movable kidney which are giving rise to symptoms, and these may be either acute or chronic.

Acute Cases.—To these the name of Dietl's crises has been applied. They are produced by strangulation of the renal vessels owing to rotation of the kidney, which may also become incarcerated in its abnormal position.

Treatment.—The patient must be put to bed, and warmth should be applied to the affected side by means of hot fomentations. The pain may be so severe that a hypodermic injection of morphia may be required, $\frac{1}{4}$ to $\frac{1}{2}$ gr. being administered, after the diagnosis has been definitely made. A purge may also be given, as the peristaltic movement of the gut thus induced may rectify the position of the affected kidney. Under this treatment the attack usually passes off within a few hours. Should it persist longer an anæsthetic may be given, and an attempt made to rectify the faulty position of the kidney by bimanual manipulation. This is sometimes successful, but in a few cases an operation may be necessary to release the kidney. At the operation the kidney should be fixed to the lumbar parietes after the faulty position has been reduced. Owing to the greatly congested and swollen condition of the organ at the time, this operation cannot always be successfully performed, in which case it should be fixed later when things have quieted down.

Chronic Cases.—It is the exception rather than the rule for a movable kidney to cause trouble, but it will be well to refer briefly to the various symptoms that may be properly referred to this condition.

1. *Pain.*—This is commonly a dragging pain in the back, most noticeable in the posterior renal angle. It may also be met with anteriorly in the hypochondrium, exceptionally it is

complained of extending down the back of the thigh and leg.

2. Dyspeptic symptoms are fairly common.

3. Frequency of micturition often occurs.

4. More serious symptoms are referable to the production of a hydronephrosis, which may become infected, and thus give rise to pyonephrosis.

5. Occasionally there may be produced dilatation of the stomach, due to the formation of adhesions in connection with a movable kidney.

Treatment may be either operative or palliative.

The following points serve as indications for operative treatment.

1. Cases in which acute symptoms such as pain with hæmaturia and vomiting occur.

2. Cases in which there is evidence of pathological changes in the kidney as a result of its mobility. Such are hydronephrosis, intermittent albuminuria, and the presence of casts in the urine.

3. Cases in which the kidney is mechanically causing pathological changes in other viscera, *e. g.* dilatation of the stomach, or duodenum, and occasionally jaundice.

4. Cases in which chronic dragging pain exists, and which cannot be relieved by the palliative treatment to be presently described.

A certain degree of neurasthenia, which exists very commonly in these patients, does not contra-indicate operation, but if an operation be performed simply for the neurasthenic condition in the absence of any of the special indications for operation mentioned above, the results will be disappointing and the recommendation of operative treatment cannot be justified on any grounds. I have seen several patients who have been so treated without the smallest benefit to their neurasthenic conditions, but with the additional disadvantage of having a scar in which to feel pain and discomfort.

Palliative Treatment.—In a large number, perhaps the majority, of patients in whom a movable kidney is giving rise to symptoms the wearing of a suitable kidney truss or special corset will, as a rule, prove quite effective. Many of the patients have lost flesh recently and are in a poor state of health. There is accordingly an excessive reaction to sensory impressions which they would disregard if in a better state of health. In such a patient a rest cure should be obtained under the most favourable conditions, and after this a belt or corset ordered. The nutrition of the patient must be improved by giving extra milk, cod-liver oil and malt, if these can be well taken. Sufferers from movable kidney are almost always very constipated, so that careful attention to the bowels will be required.

A word or two is necessary on the important question of the choice of a truss or corset. Many of the articles advertised for this purpose are of no use whatever, and may do more harm than good by allowing the kidney to descend and then fixing it in this abnormal position. Most careful fitting is necessary, and a good deal of patience must be exercised on the part of the patient, doctor and the truss-maker if the instrument is to be a success. The instrument made by Ernst is very efficient, and as it is light it can, as a rule, be worn without much discomfort by the patient. The truss need only be worn during the day and should be applied by the patient before getting up in the morning. She must adjust it while in the recumbent position, preferably with the pelvis raised on a pillow. The loin should previously have been grasped by the fingers and thumb, to make sure that the kidney is in its proper position before the truss is applied.

As a result of wearing an adequate truss or corset the expectation is that the symptoms will be relieved. Experience shows that after a year or two, during which the truss has been worn, it may be possible to relinquish it without recurrence of symptoms. In the case of men who have to lead an active life, and in whom movable kidney is often due to trauma, it is probably better to advise operation at once, rather than to rely on a kidney truss.

For the details of the operative technique the reader is referred to works on operative surgery.

C. M. H. H.

KIDNEY DISEASE IN PREGNANCY

Introduction.—Under this heading will be discussed the treatment of the Kidney of Pregnancy, Eclampsia and Pyelitis during Pregnancy.

It must be remembered that the kidneys may show pathological changes, and albumen may be present in the urine during pregnancy in several other conditions, such as pernicious vomiting, icterus gravis, and hydatidiform mole, but in these conditions the kidney lesions are of secondary importance and it would be out of place to consider their treatment here.

Two great groups of kidney disease in pregnancy can be distinguished.

Group I, in which the patient has had no previous kidney trouble, and in which the disease is entirely due to the pregnancy. These are cases of true toxæmia.

Group II, in which the patient has suffered from previous kidney symptoms which are made worse by the patient being pregnant. The pregnancy is an accidental complication of an old-standing disease.

In dealing with a case of kidney disease in pregnancy, therefore, it is necessary clearly to

distinguish between these two groups. Failure to do so has led to much confusion and divergence of opinion upon the subject, and to errors in prognosis.

The distinction may be made by a consideration of the following points. In some cases, however, it is extremely difficult to make the distinction, and of course it is possible that a true toxæmia may be superimposed upon a case of old kidney disease so that the two conditions may exist together in the same case.

In *Group I* no history of scarlet fever or diphtheria is often obtainable, nor of any previous symptoms of kidney disease; there are no evidences of cardiovascular change; the blood pressure is usually increased, but it falls quickly after delivery; the patient is usually a primipara; the symptoms appear towards the latter months of pregnancy; the œdema is most marked about the legs and vulva; the eyes show no changes except intense œdema and partial detachment of the retina, retinal hæmorrhages are not common, and these changes totally disappear after the patient recovers; the urine is markedly diminished in amount and may contain much albumen (principally paraglobulin), some casts, and a diminished amount of chlorides—further, it may contain acetone and diacetic acid; the total nitrogen excretion is lessened, the percentage of urea may be lowered, and there may be a rise in the amount of the ammonium salts and undetermined nitrogen; the alkalinity of the blood is less.

In *Group II* there is usually a history of scarlet fever or of diphtheria and of a previous attack of kidney disease; there are evidences of cardiovascular changes, the arteries may be thickened, the heart hypertrophied and the blood pressure increased; the patient is usually a multipara; the symptoms appear early in the pregnancy; the œdema is most marked about the legs and face; the eyes may show evidence of albuminuric retinitis; the urine before the pregnancy may have been increased in amount, and it contains albumen and epithelial casts, but no acetone or diacetic acid. The cerebrospinal fluid may be shown to contain urea.

The Treatment of Group I

(*The Kidney of Pregnancy—Eclampsia*)

The present-day treatment of this group of kidney diseases in pregnancy is based upon the fact that they are regarded as examples of a true toxæmia.

The toxæmic theory may be stated briefly thus. It supposes that in health the waste products or toxic substances are eliminated either directly by the alimentary canal, the kidneys, the sweat glands, and the lungs, or by transformation within the body into non-toxic substances chiefly by the liver. During normal pregnancy the amount of waste products is increased by those derived from the ovum. Two factors, therefore, come into play, the amount of waste products, and their elimination. Should the amount of these waste products be much increased, or the overworked functions of the excretory organs break down, then a condition of toxæmia or auto-intoxication results.

The toxæmic theory is not a proved fact, but it is now generally accepted, although the toxin or toxins have not yet been isolated or demonstrated and their nature and mode of action remains unknown. The known facts point to the presence of a toxin circulating in the blood of the pregnant woman, and further that this toxin is derived from the epiblastic covering of the chorionic villi, and it is upon this view that our treatment is based.

The toxæmia may manifest itself clinically in various ways. The boundary line between physiological and pathological processes is ill-defined in pregnancy. It is now believed that many of the minor ailments of pregnancy are toxic in nature, *i. e.* pruritus, salivation and vomiting. These do not manifest kidney changes and so will not be considered here. More severe manifestations of toxæmia are the kidney of pregnancy, eclampsia, pernicious vomiting and acute yellow atrophy; these show kidney changes, but in all except the kidney of pregnancy and eclampsia the changes are subsidiary and so the treatment of these two only is considered here.

1. **The Kidney of Pregnancy.**—A patient suffering from this condition usually complains of symptoms during the latter months of pregnancy. She may complain of vomiting, headache, dimness of vision and swelling of the legs, and on examination the urine contains albumen.

Prophylactic Treatment.—Every pregnant woman, and especially primigravidæ, should have the urine examined regularly twice a month during the latter half of pregnancy. The urine is to be tested for albumen. Some authorities attach great importance to the percentage of urea, but it is doubtful whether this carries the significance attributed to it. Only when we also know the total nitrogen and ammonia nitrogen can we get satisfactory chemical evidence of the approach of toxæmia. (See also article on *Chronic Nephritis.*) The patient should be warned to notify her doctor if she has headache, œdema or dimness of vision, and if she passes only small amounts of urine.

Should these symptoms be present or the urine be diminished in amount and contain albumen then treatment must be at once begun.

Curative.—The indication is to get rid of the

toxin which is supposed to be present in the mother's blood. This can be eliminated by the kidneys, bowels and skin.

The patient is placed in bed because there a more accurate knowledge of the intake and output can be obtained. The diet must be light, nitrogenous food is to be avoided in order to save the extra work of the liver and kidneys. At first she may be allowed milk, cocoa, bread and butter, custard, eggs and fish. She must not have alcohol, rich food, soups, meat extract, any meat or vegetable.

The effect of this diet upon the symptoms must be watched, and in more severe cases the diet must consist only of milk—two quarts in the twenty-four hours—and the patient encouraged to drink as much barley-water and imperial drink as possible with the object of flushing the kidneys. Some simple diuretic such as Pot. Acetate and Spiritus Ætheris Nitrosi may be given.

In order to eliminate the toxin by the bowel a free evacuation should be obtained daily—for this magnesium sulphate is indicated, because of the fluid motions it causes, by which means it is possible that some of the maternal toxins may be disposed of.

To combat the acidosis found in toxæmic cases, glucose 5 per cent. may be given. A pleasant way is to add to it the juice of a lemon, which is known as glucose lemonade; if the patient feels too sick to retain by the mouth it may be given per rectum and also as much saline as possible.

Under this treatment there is usually a rapid improvement, the œdema subsides and the urine increases in quantity and contains less albumen. An index to the degree of improvement is given by a urine chart—showing the percentage of albumen, amount of urea and amount of urine passed daily.

Should the symptoms persist and there be no improvement in the condition of the urine—the urine become scanty, contain more albumen (preferably estimated by Aufrecht's method), and the amount of urea diminish, then the pregnancy should be terminated in order to free the mother's body of the source of toxin. The mother's interests mainly are to be considered, for the fœtus often dies in utero—and by terminating the pregnancy there is less danger of the onset of ante-partum hæmorrhage and eclampsia. This is done by the introduction of bougies between the membranes and the uterine wall. Contractions appear in from twelve to seventy-two hours, and when the cervix is fully dilated, the forceps should be applied, provided the vertex presents and is well in the pelvic cavity; otherwise version should be performed and the child allowed to be born slowly and not immediately delivered. All manipulations must be performed gently for fear of causing stimuli which may in their turn give rise to eclamptic convulsions. As little chloroform as possible should be given, for lesions similar to those of eclampsia have been found in the liver in cases of prolonged chloroform anæsthesia. To avoid this the anæsthesia may be obtained by the extra dural sacral—not spinal—injection of stovain, or by the administration of ether by the open method.

2. **Treatment of Eclampsia.**—*Prophylactic.*—Prophylactic measures are of the greatest importance. They have been already considered under the treatment of the *Kidney of Pregnancy*, in which condition, indeed, our chief aim is to guard against the onset of eclampsia.

Should the symptoms not improve or should the patient become progressively worse, then the onset of eclampsia must be regarded as imminent.

Usually clear indications of its onset are given by the persistence of the headache; an increase in the amount of œdema; the presence of eye changes such as dimness of vision, flashes of light in front of the eyes and even sudden blindness; by epigastric pain, vomiting, giddiness and muscular twitchings. The urine becomes scanty in amount, the albumen much increased while the urea is less.

By the employment of precautionary measures the liability to eclampsia is much diminished, but we are not able to claim that it can be absolutely prevented. Eclampsia may still occur even after all the symptoms have subsided, and even with scarcely any warning. I know of a patient whose first symptom was sudden blindness before the appearance of albumen in the urine.

Curative Treatment.

1. *Medical.*—On account of our small knowledge as to the causation of eclampsia, our aims are in the main still empirical and symptomatic.

The treatment may be considered under the following heads—

(a) *The Treatment of the Fit Itself.*—The patient, if possible, should not be moved during the fit, but allowed to rest where she lies in order to obviate all unnecessary handling and stimulation.

A gag must be placed between her teeth. If no real gag is at hand then a spoon or some similar firm object with a handkerchief wrapped round it will answer the purpose. This is done in order to prevent the patient from biting her tongue during the convulsion.

The head must be turned on to one side in order to prevent blood and saliva from entering the air passages with the risk of suffocation immediately, or of septic broncho-pneumonia at a later date.

The patient must be gently restrained from

injuring herself, and a pillow be placed beneath her head.

The clothing must be loosened in order to allow as much air entry as possible.

The question of the administration of chloroform or morphia during the fit is discussed later.

(b) *The Prevention of the Recurrence of the Fit.*—The patient must be put to bed, her clothing being gently removed and no irritating material placed next her skin. The bedroom itself should be in the quietest part of the building, the blinds should be drawn down and no bright light or sudden noise be allowed to penetrate into the room. No one should be allowed to see the patient other than the doctor or nurse. All unnecessary manipulation must be avoided, such as vaginal examination or the use of catheter or enema.

The diet must be the same as for a severe case of the "Kidney of Pregnancy." If the patient be unconscious the feeding should be done by means of the nasal tube.

Various anæsthetic or sedative drugs are given to prevent the explosions of nerve energy which originate the convulsion.

Of such drugs we must consider—

Morphia.—This drug is simple of administration and is pleasanter to both patient and doctor than chloroform; it tends to retard protein metabolism and so may help by diminishing the formation of toxins; it allays restlessness; it diminishes arterial tension and has a marked effect upon the fits. But it tends to weaken the uterine contractions and so delays labour.

It is to be recommended in ante- and postpartum cases of eclampsia, and especially if there is no sign of coma and the pulse is full and bounding.

It is best given in full doses of $\frac{1}{2}$ gr. subcutaneously, together with atropin sulphate $\frac{1}{100}$ gr., on account of its depressant action upon the respiratory centre. This dose may be repeated if necessary until 2 gr. of the morphia have been administered.

Chloroform.—The drug acts quickly, is rapidly eliminated and can be administered to patients who are unable to swallow. During the actual convulsion it is not of much value as the patient is scarcely breathing.

But sometimes it has no apparent influence in controlling recurrence of the convulsions, and its prolonged administration is contraindicated not only because it is troublesome to give, but because it may set up lesions of the liver similar to those found in eclampsia.

It may be administered in two ways. The first is to give it at intervals to ward off an oncoming convulsion, watch being kept for signs of this, such as widening of the pupil and fibrillary tremors of the muscles of the face. The drawback to this method is the length of time taken up and the risk of causing hepatic lesions. The second is to give it when vaginal or intrauterine manipulations are necessary. It is generally given in intrapartum eclampsia to control the convulsion, and for obstetric manipulations.

Chloral Hydrate and Bromide of Potassium.—These may be given as substitutes for chloroform or morphia, or in combination with small doses of morphia.

If given by the mouth full doses should be administered, such as 30 gr. of chloral and 15 gr. of bromide every hour until four doses have been taken. Should the patient be unconscious they may be given in double the doses by the rectum combined with starch mucilage. But should there be no good effect at the end of the four doses their administration is better discontinued.

Lumbar Narcosis.—Spinal anæsthesia as well as lumbar puncture followed by the removal of some of the cerebro-spinal fluid have proved ineffectual in controlling the occurrence of the fits.

Veratrum viride has been recommended for its action as a vaso-dilator and diuretic, but on the other hand it is a cardiac depressant and its use is by no means free from risk. The dosage is 15 min. every half hour until the pulse-rate falls to sixty beats a minute. It may be given as veratone, 1 c.c. intramuscular injection if the patient be unconscious.

Thyreoid Extract.—Extracts of the gland may be given, as according to some an insufficiency of the thyreoid internal secretion is regarded as the cause of eclampsia. Whether this be so or not is open to doubt, and where relief appears to have followed its use it may be due to its vaso-dilator and diuretic action.

Pituitary extract has also been recommended, but so far the results are not sufficient for us to draw any definite conclusions.

(c) *The Elimination and Dilution of the Toxins.*—The toxins may be eliminated by the bowel, by the skin, and by the kidneys.

(i) *By the Bowel.*—The special drugs which are indicated for this purpose are castor oil, jalap and magnesium sulphate. If the patient is unconscious 2 min. of croton oil should be given in a small piece of butter in order to protect the buccal mucous membrane. These drugs are of value in that they not only cause a free evacuation from the bowel and so dispose of some of the toxins, but they also tend to lower the increased blood pressure.

(ii) *By the Skin.*—It is usually recommended to make the patient perspire by the free use of hot packs or the vapour bath, and by drinking large quantities of fluid, or the administration of saline per rectum.

Of these methods the drinking of large quantities of fluid where possible is the best, for the use of the others entails a good deal of movement and manipulation, and these may bring on the convulsion. Further, as Bumm has pointed out, it would appear as if sweating in some cases has caused stronger convulsions, deeper coma and a higher degree of fever, and it is not clear that the supposed eclampsia toxin leaves the body with the sweat. It may be that sweating makes it more concentrated.

Pilocarpin should certainly not be given on account of its action upon the bronchial glands and the risk of pulmonary œdema.

If the temperature reach as high as 105° F. it should be reduced by the tepid bath at a temperature of 70° to 80° F. until the rectal temperature falls 2° to 3°. Profuse sweating follows, and the temperature will continue to fall.

(iii) *By the Kidneys.*—Large quantities of bland fluid rather than active diuretics should be given by the mouth; barley-water, water, imperial drinks are all suitable. To counteract acidosis, glucose 5 per cent. may also be given, preferably with some lemon-juice added. Subcutaneous saline should be given, but this is contra-indicated in the presence of fits or if the patient is restless. The saline should then be administered per rectum in large quantities, or intravenously. It is usual to add a drachm of sodium acetate to a pint of the saline in order to increase the alkalinity of the blood, which is diminished in eclampsia from the normal 0·202 gm. per cent. to 0·153.

The saline is to be recommended, for it dilutes the toxin, causes diaphoresis, and some hours later acts as a diuretic.

(iv) *By venesection.*—The toxins may be lessened and the blood pressure lowered by the removal of some of the patient's blood from the median basilic vein. This may be done as a preliminary, also, to the intravenous *infusion of saline,* in order not to raise the blood pressure. The removal of blood is to be recommended if the patient is cyanosed, shows signs of œdema of the lungs and has a full bounding pulse with raised blood pressure. It is contra-indicated if the patient is anæmic, feeble and has a low blood pressure. From 10 oz. to 1 pint of blood should be removed according to the condition of the patient. Not seldom it has been noted that the fits immediately stop and the coma dissipates. Lichtenstein records that one venesection in 54 per cent. of cases was followed by cessation of the fits.

Zweifel has recently shown the blood is more concentrated in eclampsia, and he goes on to state that it "is difficult by means of therapeutic statistics to speak of proof; but most of my colleagues will hold it of importance if from my actual experience I affirm that the removal of blood has in no case done harm, and that it has very often appeared to save life."

Further it must be remembered that the coma may be deepened owing to CO_2 poisoning, for during the convulsions the air entry is interfered with, and at all times there is some obstruction from the presence of mucus. Removal of some of the blood and the administration of oxygen are to be recommended if the patient is cyanosed. Artificial respiration is necessary in some cases.

Serum Treatment.—This is recommended on the supposition that the toxins of pregnancy call out ferments in the normal patient's blood, which are able to counteract them. Should these ferments not be produced in sufficient quantity then the toxins are unchecked and a condition of toxæmia will result.

These ferments may be artificially supplied by the administration of human serum from the blood of normal pregnant women, and also it is claimed from non-pregnant women, or from the horse.

Good results are recorded by Fieux and Gui from serum administration given in doses of 15 to 25 c.c. either subcutaneously or by the mouth, in cases of hyperemesis gravidarum, which, like eclampsia, is regarded as a manifestation of the toxæmia of pregnancy. It has been recommended on this analogy, but up to the present evidence in its favour is inconclusive.

2. *Obstetrical Treatment.*—There are two entirely and strongly opposed views as to this. On the one hand, it is claimed that no obstetrical manipulations are necessary unless the woman is in labour or prolonged medical treatment fails; the other view is that on the occurrence of a fit the pregnancy must be terminated at once.

The former view is based upon the statements that the convulsions are not due to the labour, they occur apart from labour and the labour pains do not stimulate them, and that according to Herman they continue in 57 per cent. of cases after labour. Therefore the main thing is to treat the fits by medical measures and not to hasten delivery.

The latter view is based upon the supposition that the condition is due to toxæmia and that the toxin is derived from the ovum. Therefore the toxin should be removed by the removal of the ovum, and as there is still much toxin within the maternal system even after the expulsion of the cause convulsions may still follow, so that the medical treatment must be continued even after the delivery. If we rely upon statistics of the proportion of cases which have no more convulsions after the birth, it is 66 per cent. according to Zweifel; he also finds a maternal mortality of 28·5 per cent. by the

expectant treatment as against 11·25 under active obstetrical measures.

Most investigators now favour the second view. In the absence of a fit treatment should be by the medical measures already discussed, but if the symptoms become worse, or if a single fit occur, then prompt delivery should follow. In our methods of hastening delivery we consider the interests of the mother first, for the child is often premature, diseased and malformed.

If the Patient is not in Labour.—The cervix should be dilated by metal dilators until it will admit a Champetier de Ribes' bag, and when it is fully or almost fully dilated the labour should be terminated by the forceps or by version.

If the cervix be extremely tough and undilatable then either vaginal or abdominal Cæsarean section should be performed, if a competent operator be available and the conditions are suitable. Abdominal Cæsarean section is preferable, especially if the child is large and the vagina small, but the vaginal method may be practised if the child is small —before the twenty-seventh week—and the vagina large.

The anæsthetic to be used for these manipulations should be ether by the open method, provided that there is no evidence of pulmonary œdema, but if this is present chloroform should be used in as small a quantity as possible.

If the Patient is in Labour the treatment is much simpler. If the cervix is not fully dilated it should be dilated by the digital method. If the head presents and is not too high apply the forceps; if this instrument is contra-indicated perform version and bring down a leg.

During the management of the third stage some degree of bleeding may be beneficial where the patient is cyanosed and has a full pulse.

After the delivery the medical measures against the toxæmia must be continued. Special attention must be paid to the increased liability of infection locally, to septicæmia, and to the signs of the onset of puerperal insanity.

The question may arise as to future pregnancies. To this we answer that the attacks are seldom repeated, especially if the attack has occurred in a primapara. The patient must, however, be warned that there is some risk.

3. *Surgical Treatment.—Decapsulation of the Kidneys* has been recommended in cases of total or almost total suppression of urine in order to relieve the venous stagnation within the kidneys. At present there is not sufficient proof of this line of treatment to allow us to judge of its merits, but any such procedure is attended by many and severe manipulations, and, it must be remembered, the risk of infection is greater in eclamptic patients.

The Treatment of Group II

(*Pregnancy with Chronic Nephritis*)

The treatment of chronic nephritis is considered separately in the present work (see p. 333). Only the following points from the obstetrical point of view, therefore, need to be added.

It may be supposed that the previously damaged kidneys have been able to perform their function satisfactorily so long as no added strain was put upon them. When the patient becomes pregnant this added strain is supplied, for now not only the maternal but the fœtal products of metabolism have to be eliminated; they are unable to do so and consequently a breakdown in their function and an increase in the amount of permanent kidney lesion result.

If this view of the pathology of the condition be correct, then it will be readily understood that should palliative measures not be attended by rapid improvement, the pregnancy should be terminated. Expulsion of the ovum is usually followed by marked improvement in the symptoms. Further, the life of the child is so precarious in this condition that our treatment must be primarily in the interests of the mother.

Should the medical man be asked to give his opinion as to the advisability of marriage, he must remember he has no right to forbid it. He should point out the facts to the individuals concerned and explain the risks.

The patient is usually worse in a succeeding pregnancy, and the symptoms earlier in their appearance.

Sometimes, however, patients who are known to be the subjects of chronic nephritis have passed through successive pregnancies and survived.

The Treatment of Pyelitis during Pregnancy.—This can no longer be regarded as a disease special to pregnancy. It is well known to occur in other conditions; it occurs quite commonly in young children, and it may do so also in men. The treatment of this condition is considered on p. 350; here we are mainly concerned with its relation to pregnancy and to the puerperium.

Medical Treatment.—The patient should be placed in bed. It is usual to direct her to lie upon the opposite side to that affected in order to drain the pelvis of the affected kidney. This is based upon the view that the pregnant uterus is compressing the ureter—usually the right—against the brim of the pelvis. That this view is really correct is open to doubt. In many cases the right ureter shows a dilatation from this point upwards, but cases have occurred in which the dilatation has been along the whole length of the ureter from its insertion into the bladder. At any rate such a position is good

in that the diseased kidney is uppermost and is therefore less pressed upon.

The symptoms certainly subside more rapidly if the patient is confined to bed.

The diet should consist of milk, cocoa, custard, bread and milk and small quantities of eggs and fish in order not to overwork the damaged kidney structure.

The kidneys should be flushed through with large quantities of barley-water or imperial drink. Urinary antiseptics such as urotropin or helmitol should be given by the mouth. Urotropin is best given in the powder form, 5 gr. with 20 to 30 gr. of acid sodium phosphate three times daily.

The bowels must be regulated, especially as constipation or colic so often precede and accompany the attack.

Serum and vaccine treatment have so far proved disappointing on the whole. The commonest causal organism is a coliform bacillus. The reason why an anti-coli serum fails may lie in the fact that the Bacillus coli group contains so many organisms which vary slightly in their biochemical reactions and the serum may not be suitable for the particular case, and further it is open to doubt if the Bacillus coli really does produce any antibody. Vaccines must, of course, be autogenous. The dosage is from 10 millions increased up to 100 millions repeated with forty-eight-hour intervals.

A sensitised vaccine is recommended also, in which case the dose begins with 100 millions and is repeated at twenty-four-hour intervals until three doses have been given.

The results of vaccine treatment are not conclusive. It is difficult to be sure that any observed improvement is really due to the vaccine, for the improvement occurs suddenly very often without any such treatment or before the course of vaccines has had time to be completed. This much may be said, that the symptoms do appear to be kept in abeyance as long as vaccines are administered, although it is interesting to note that the organisms may still be found in the urine sometimes for many months afterwards.

Operative Procedures.—In the majority of cases medical treatment alone is sufficient, a marked improvement taking place within about ten days.

In cases where no such improvement is manifested, Stoeckel has recommended irrigation of the renal pelvis. There are obvious objections to such a procedure, nor is it probable that any benefit would follow, because in severe cases not only is the kidney pelvis affected but the kidney substance contains many small abscesses. Two fatal cases seen by the writer both showed these lesions at the post-mortem examination.

If, after ten days' treatment upon the lines already indicated, the patient is no better, the temperature persists and the pulse-rate is increasing, the question of operative interference arises. The case is complicated by the pregnancy, for any operation upon the kidney is likely to be followed by abortion. It is better to drain the kidney by diminishing the bulk of the uterus by terminating the pregnancy. This is most conveniently done by the introduction of bougies between the membranes and the uterine wall.

But such a procedure should not be undertaken lightly. It is very seldom necessary, and does not always succeed in bringing about any improvement in the symptoms.

Finally, we may remark as to preventive treatment that the condition may occur during the puerperium, therefore all unnecessary use of the catheter should be guarded against.

J. D. B.

ESTIMATION OF THE RENAL ADEQUACY

Unfortunately it must be admitted that there is at present no really satisfactory method of estimating the functional power of the kidneys, and yet, with the exception of the work of the heart, there is hardly a question on whose answer so much of importance to life depends. In the present very short epitome I must confine myself simply to those tests which seem to me to be of practical interest.

What are the Clinical Signs of Renal Inadequacy.—These are agreed on—the patient's skin is loose and dry, his complexion dull yellow, conjunctivæ dull and somewhat œdematous, tongue dry and somewhat glazed, he complains of constant frontal headaches, and may admit a certain amount of polyuria, his urine may be of low specific gravity and show a cloud or haze of albumen. This is all that can be obtained—trivial symptoms one may say, and yet an operation on the urinogenital tract (or elsewhere) in such a patient will almost certainly be fatal.

Tests of Renal Adequacy.—Here we have to decide on (1) the adequacy of both kidneys, (2) that of either kidney separately, and of these the second is the question which will more frequently present itself for decision. It is now generally admitted that all attempts to separate the urine coming from either ureter *in the bladder* and to collect it separately are entirely fallacious and should be discarded. Thus at present the only satisfactory method of examining the urine from either kidney is by catheterisation of the ureters by ureteral catheters passed under the direct view of the cystoscope. It is clear that this method can only be used by the expert, further, that it requires continued exposure as the catheters

must be left in the ureters for at least two hours (no anæsthetic is necessary).

Radiography.—Reliable radiographs of the kidney area will at any rate show us the outline of a normal kidney and may prove the presence of a normal kidney free from calculi on the opposite side to a diseased kidney.

Pyelography.—Vœlcker first attempted the injection of the pelvis of the kidney with a 2–5 per cent. solution of collargol, a soluble organic salt of silver, which casts an X-Ray shadow. Thomson Walker uses a 10–20 per cent. solution of collargol; of this solution he injects about 20 cc. from an all-glass syringe held from six inches to one foot above the level of the body into each ureteric catheter (the catheters are also opaque to X-Rays). On the first appearance of symptoms of discomfort in the renal regions the injection is stopped and an X-Ray photo taken. By this means the permeability of the ureter and the size, position, etc., of the pelvis of each kidney may be defined.

Injection of Phloridzin.—Ten milligrams of phloridzin are injected subcutaneously into the buttocks; sugar should appear in the urine of a healthy person in fifteen minutes—occasionally up to thirty—after the injection. The amount of glycosuria is usually 1–2 gm. of glucose, and it should have passed off in from 2–2½ hours. In urinary obstruction there is diminished elimination of sugar and in badly damaged kidneys sugar may be absent.

Injection of Methylene Blue.—Fifteen minims of a 5 per cent. aqueous sterilised solution of methylene blue are injected into the buttock. The methylene blue is excreted first as a chromogen, and later as methylene blue itself. The chromogen (which turns into methylene blue when boiled with acetic acid) should appear in the urine in from 15–20 minutes, soon after this time the excretion of unaltered methylene blue should begin; it should be at its maximum in from 4–5 hours, and should have disappeared in from 40–50 hours. This test cannot be relied on, for in acute or subacute nephritis the rate of methylene blue excretion is entirely unaffected.

Injection of Phenol-sulphone-phthalein.—Six milligrams are injected hypodermically, the urine from the ureteric catheters is allowed to drop into a 25 per cent. solution of potash; as soon as the drug begins to be excreted a pink colour is obtained which gradually deepens into red. The amount of the drug excreted is estimated by a colorimeter. "In normal cases the colouring matter is said to appear in from five to ten minutes, 40–60 per cent. of the drug is excreted in the first hour, 20–25 per cent. in the second, and 60–85 per cent. in the first two hours."—(Thomson Walker.)

Injection of Indigo Carmine.—0·16 gm. of indigo carmine is dissolved in sterilised water and injected hypodermically; in about ten minutes the urine is coloured, and then passes through various stages of green to blue, the greatest amount being excreted in about an hour after injection; the quantity can be roughly estimated by the eye or more accurately by a colorimeter.

"Delay in the appearance and a feeble staining of the urine are signs of disease."—(Thomson Walker.)

Examination of the Urine of the Healthy Kidney.—A ureteric catheter can be passed into the pelvis of the (presumably) healthy kidney and the urine collected for 2–2½ hours and carefully examined. In the middle of the process a cup of hot tea or other diuretic may be given. After the collection, urotropin and a diuretic should be given, and the patient should remain in bed for thirty-six hours. This method is obviously not free from risks.

It will be readily seen from the foregoing very brief statement that the various methods of estimating renal adequacy are highly complicated, both from the chemical and surgical points of view, and it must be admitted that it is unsafe to rely on any one of them—in a doubtful case it is important to have the results of all of them before the surgeon for final decision. J. K. M.

DISTENSION OF THE PELVIS OF THE KIDNEY

Non-suppurative Hydronephrosis.—While it must be admitted that treatment of non-suppurative distension of the kidney must be confined to surgical measures only, and these of a somewhat technical character, it is of practical interest to note that much progress has been made from those by-no-means far-off days when the hydronephrotic kidney was hurriedly removed or perhaps tapped again and again through the loin.

More recently the pelvis was drained through the loin, and as it came to be admitted that the mobility of the kidney was at times an indirect cause, nephropexy or fixation of the kidney was performed.

At the present time surgery is directed towards the preservation of the kidney by discovering and treating the cause of the distension at as early a stage as possible.

As to the *causes of hydronephrosis* we must remember that in a considerable proportion of cases examined post-mortem no cause is discoverable (in fourteen out of nineteen cases, Herringham), in the remainder obstruction of some kind is found and this most frequently is advanced malignant disease of the female pelvic organs.

It is well known that hydronephrosis may be *temporary and intermittent* or *permanent*.

Temporary Hydronephrosis.—In all such cases expert surgical advice should be sought, for here the cause may be (1) kinking or even twisting of the ureter of a mobile kidney, which comes to lie in loose tissue instead of fairly firm retroperitoneal fat. Here fixation of the kidney should provide a cure.

(2) Intermittent valvular obstructions by calculi, folds or even small growths of the calices of the kidney—towards the renal orifice of the ureter. Here recognition of the cause provides the proper line of treatment: stones and growths are removed by horizontal incisions through the pelvis of the kidney, and in those cases where there is complete obstruction to the ureter a lateral or end-to-end anastomosis of the ureter to some other part of the pelvis should be undertaken.

Permanent Hydronephrosis.—This is most frequently due to complete obstruction of a ureter by (1) (and most frequently) malignant disease—usually in the pelvis. Here treatment will most probably only consist in establishing a renal fistula in the loin in the hope of preserving the still functional cortex—although the extent and progress of the disease may make even this undesirable; it is to be remembered that in some early cases of pelvic carcinoma the ureter has been successfully cleared from the growth.

(2) By calculi obstructing the ureter in any part of its course. Here it is worth remembering that (*a*) the degree of the obstruction by no means corresponds to the size of the calculus—rather the reverse; (*b*) that such calculi cannot be excluded by radiography even in the hands of the most expert; (*c*) the recently adopted injection of a ureter with collargol (an organic compound of silver opaque to X-rays) will show the position of an obstruction to the ureter in any part of its length and clear up the diagnosis of a doubtful shadow, as well as prove the presence of a normal ureter on the opposite side.

Calculous obstruction is obviously to be dealt with by removal of the cause, suture of the ureter or pelvis of the kidney, with artificial enlargement of the structure, or anastomosis if necessary.

(3) Due to aberrant branches of the renal artery—a by-no-means uncommon cause. In this condition the lower aberrant branches appear to pass from the aorta over the ureter, thus actually constricting it (Mayo), while aberrant branches to the upper pole of the kidney would appear to cause a torsion of the whole organ. These aberrant branches can be readily felt through a lumbar incision, clamped and ligatured—usually with a most satisfactory result.

(4) Due to ureteral strictures and much rarer developmental causes.

Thus the treatment of hydronephrosis is essentially surgical; yet, nevertheless, successful *surgical* treatment rests on the early diagnosis of the practitioner, for the sooner it is diagnosed and the cause removed the better the chance of saving the kidney. In early cases the history may help the practitioner, but alterations in the *quantity* of urine are delusive. There is no pain unless there is a moving calculus or superadded septic infection.

If the practitioner is in any doubt as to the presence of *any* enlargement in the renal region he will do well at once to obtain the evidence (*a*) of X-rays, (*b*) of cystoscopy and collargol intra-ureteral injection by an expert, while an estimation of the efficiency of the sound kidney by pyelography, phloridzin and methylene blue tests should be conducted as a matter of routine.

J. K. M.

GENERAL INFECTIVE CONDITIONS OF THE KIDNEY

Pyogenic Infections

Pyogenic infections of the kidney may best be considered in the following divisions—

(*a*) **Pyelitis.**—Here the suppurative changes are usually confined completely to the pelvis of the kidney.

(*b*) **Pyelonephritis.** — Here the infection has certainly attacked the pelvis of the kidney, but in addition it has also spread into the cortex and there caused diffuse inflammation and multiple abscesses; on the other hand, in some cases it is equally reasonable to suppose that the infection has spread from the cortex to the pelvis.

(*c*) **Pyonephrosis.** — Here obstruction to the ureter, usually by a calculus, is superadded to the original infection, the infective process rapidly destroys the kidney substance, which is meanwhile being distended by pressure, and unless the obstruction is relieved at an early stage, the kidney is soon changed into a large thin-walled bag of pus and the suppuration spreads into the perinephric tissues.

Source and Cause of Infection

1. **Embolic.**—There is no doubt that organisms can be brought into the kidney by the circulation; in health there is little doubt that large quantities of organisms are excreted by the kidneys, some alive, but most of them either dead or with their toxicity greatly reduced: in depressed conditions of the general organism or of the circulation; we know that B. coli is able to pass in large numbers from the intestine into the intestinal blood and lymph vessels, and in this way it reaches the kidney.

2. **Ascending Infection** from the bladder along the ureter. This is probably a far rarer

source than was once supposed, it may occasionally be the cause of pyelitis in young female children, but it is far more common in the ascending pyelonephritis of long-infected bladders and in pyonephrosis.

3. **Lymph Infection.**—This is probably by no means uncommon in pyelitis, for the lymph vessels of the pelvis of the kidney have free communication with the lymph vessels of the colon. (Thomson Walker produced a pyelitis in a kidney whose ureter was ligatured, by injecting colon bacilli into the bladder.) The cause of infection is almost always the B. coli in some form, more rarely the staphylococcus, still more rarely streptococci, proteus or the pneumococcus.

Pyelitis

It is well to insist at the outset on three points: (1) pyelitis is essentially a febrile disease; not only so, but the fever is not infrequently the only symptom discovered. The presence of fever will usually distinguish pyelitis from cystitis (scf. cystitis). (2) The amount of pus in the urine is not large, usually only a cloud or a faint haze, while in many very acute cases, and in children, there is only the condition known as bacteriuria—a faint haze consisting of myriads of coliform organisms and a few pus cells. (3) It is common in children, uncommon in adults, and common in later life.

Pyelitis in Children.—Pyelitis is common in children under twelve months, the infant becomes suddenly ill and has a rigor (a rigor in an infant is, according to many, almost pathognomonic of this infection), the temperature rises to 103°–104° F., falls within twelve hours and rises again. The child is very evidently ill, there is a good deal of twitching, but, on the other hand, vomiting is rare; female infants are usually exclusively affected. The amount of pus in the urine is microscopic, but there are swarms of coliform bacteria. The urine is in all cases strongly acid, and in some cases it produces a yellowish staining of the diapers.

Once the diagnosis is made the prognosis is invariably good and the treatment simple. Most observers are agreed that the first line of treatment should be to alkalinise the urine. This can readily be accomplished in infants under one year by giving 5 gr. of citrate of potash in syrup every two hours, at the same time giving, if possible, double the amount of fluid usually taken, *e. g.* by giving boiled water between the milk feeds. The patients are usually very thirsty and take fluids readily.

After one year 2–5 gr. of bicarbonate of soda can be added to the citrate of potash according to the age of the patient. In the majority of cases the temperature falls in between two to five days of this treatment, but the urine will be found still to contain B. coli, and it is wise to continue the treatment for fourteen days after the temperature has become normal. Curiously enough in some few cases—I do not know of any bacteriological distinction—the alkaline treatment fails, and here urotropin should be given in doses of 1½–2½ gr. every four hours up to one and a half years of age, 2 gr. up to two years, 3 gr. up to three years, etc. Here the same precautions with regard to continuance of treatment should be taken. Some have suggested instillations into the renal pelvis of argyrol or silver nitrate. I can only say that such treatment appears to me to be highly dangerous, seeing that both kidneys are nearly always affected. Moreover, for the past twelve years I have never been called in to see a case of pyelitis by my medical colleagues at Paddington Green; as they always found simple medicinal treatment to be entirely satisfactory.

Pyelitis in Adults.—This is, as I have already said, uncommon, though not so uncommon in the later years of life; it is usually of a rather different type.

1. *Mild Cases.*—As in the case of children the attack begins suddenly, usually with a rigor, and the temperature is of the same remittent type, but here acute bladder symptoms and intense pain are quite frequent and strangury occurs in 6 per cent. of the cases. The average case lasts from ten to fourteen days despite treatment. The urine is hazy and swarms with B. coli, it has usually a very characteristic and foul odour of stale fish, and it is not infrequently alkaline in reaction.

2. *Acute Cases.*—The acute cases begin very often with a sharp attack of pain closely resembling renal colic, there are a succession of rigors very often, and the blood-count shows a marked leucocytosis, hæmaturia is occasionally found early in these cases; in the worst of all, drowsiness, changing to coma and death, ends the scene. It is to be noted that relapses are quite common in adults, and that the acute and dangerous type of case is the rule in the aged. Both kidneys are usually affected.

Treatment.—The patient should be kept strictly in bed and kept warm. Milk diet should be given with fish or eggs, red meats and alcohol should be avoided. "Malt-Glidine" added to milk or Bengers' Food will be found to give the patient an admirable and refreshing fillip. The kidneys should be flushed with unirritating fluids, that is to say, the total amount of fluids taken in the twenty-four hours should be raised to 4–6 pints if possible. The fluids given should be barley water, Imperial drink, Evian, Vichy or Contrexeville water and the like, and the fluids

given should be constantly varied. Free action of the bowels is obviously desirable, and is to be maintained by senna, cascara or calomel, if necessary by salines. The reaction of the urine is a most important factor in medical treatment, for it is now well known that the so-called urinary "antiseptics" have little if any action in the presence of alkaline urine (cf. *Urinary Antiseptics*, Part II). Thus, if the reaction is alkaline, ammonium benzoate 10–15 gr., should be given every third hour until the reaction is altered, acid sodium phosphate 30 gr. to each dose may also be tried, but ammonium benzoate generally gives better results. Once the reaction becomes acid, urotropin 10–15 gr., helmitol or tetralin (10–30 gr.) should be given every three hours.

Vaccine Treatment is a somewhat controversial ground. Many do not believe in its efficacy, others—amongst them myself—have had excellent results. Out of sixteen cases in adults treated by me with autogenous vaccines the average duration of symptoms was six days after the first injection in fourteen of the sixteen; at the end of fourteen days the urine was free from coli in two. Colon bacilli were still present in both these cases (the vaccine had had no apparent effect on the symptoms); in one of these unsuccessful cases there was a bad relapse. There has been no relapse, so far as I am aware, in the others. All are agreed that the vaccine, if used, must be autogenous, for the actual strain of organism varies probably in each case, and the name of the coli group is indeed legion. I have been in the habit of beginning with 5 millions and continuing every three days, increasing by 5 millions up to 50 millions if necessary. It has been recommended to keep the patient lying on either side alternately, in order to "drain the pelvis." It seems very improbable that a mere change in position can in any way improve on Nature's arrangements. For the same reasons as in pyelitis of children, irrigation of the pelvis of both kidneys by surgical methods appears to me to be wholly inadmissible.

Pyelitis in Pregnancy.—This is dealt with more fully under the *Kidney of Pregnancy*.

J. K. M.

PYONEPHROSIS

The condition may be described as a purulent collection within the kidney which distends the kidney and forms an actual tumour.

Here, as in the case of pyelitis, infection may be either (1) from the blood stream, or (2) ascending; and it will be admitted here that ascending infection is by far the most common. It is usually due to infection of a kidney irritated by the presence of calculi which may or may not subsequently block the ureter.

In some rare cases there may be a mixed infection as the result of an original tuberculous tumour. There is usually hectic fever and there is no large quantity of pus in the urine.

It would, however, be a mistake to consider that the temperature is always raised. It has fallen to the lot of most surgeons to meet cases where there is an enormous quantity of foul pus in the kidney without any elevation of temperature, and here again an entire absence of leucocytosis is often observed, even where pus is pent up.

A distended kidney does *not* form a *fluctuating* tumour, for its peripheral as well as perinephric tissue is usually much thickened by inflammation.

Treatment of Pyonephrosis.—While depending primarily on the condition of the remaining kidney—and every care must be taken to investigate its condition by radiography and ureteral catheterisation with collargol—if the disease is unilateral, the proper treatment would be to remove the kidney. In acute cases of great distention, the kidney should be very freely opened first and drained. It has to be remembered that in over 50 per cent. of such cases a discharging sinus remains and the treatment is unsatisfactory. In such cases the remaining kidney should be removed at a second operation, the ureter ligatured as low down as possible and divided.

J. K. M.

PYELONEPHRITIS

An "*aseptic*" *form* is described as due to acute retention, chronic obstruction, or the excretion of irritants; it is characterised by thirst, dull lumbar pain, dry tongue, frontal headache, and polyuria—in fact all the usual symptoms of renal insufficiency; treatment in this form should be directed to removal of the cause, and otherwise does not differ from that of the other forms to be described. Pyelonephritis is, however, in the vast majority of cases, suppurative, and is usually caused by an ascending infection by B. coli from the bladder, although rarely there may be a unilateral infection from the blood stream.

Acute Infective Pyelonephritis.—Here, in addition to a suppurative pyelitis, the kidney substance is riddled with multiple minute abscesses, or round cell infiltrations; for practical purposes it may be considered as the finale of chronic septic cystitis with or without obstruction such as prostatic enlargement or stricture, or as the results of surgical interference in a chronic septic urinary tract. In such cases it is usually considered, rightly or wrongly, to be the result of a chill; and it generally begins with a rigor, the temperature may be raised or subnormal throughout, the patient is drowsy and

complains of backache and thirst, the tongue is dry and glazed, and there is nausea and constipation. He lies on his back with his legs drawn up, the abdomen is rigid and distended, there is tenderness over the kidneys, and sometimes one kidney may be felt enlarged. He passes a considerable quantity of urine containing pus, most of which probably comes from a septic cystitis. Soon the drowsiness increases, vomiting, hiccough and muttering delirium set in, convulsions are rare, suppression of urine now occurs, the drowsiness changes to coma, and within twenty-four hours death ends the hopeless scene. Where a cure can hardly be said to exist it will be admitted that prevention is the better part, and thus it behoves the sufferer from urinary obstruction or cystitis to seek and obtain adequate treatment at an early stage before it is yet too late, while it is equally important for the surgeon to abstain from brilliant operative measures in debilitated subjects with chronic septic cystitis with obstruction and content himself with draining the bladder first.

Treatment.—The only possible line of treatment that can be adopted once acute ascending pyelonephritis has set in, is to attempt to keep up or to restore the excretory work of the kidneys. As a first measure dry cupping should be applied to the loins, followed by turpentine stupes and a hot pack, the bowels should be made to act freely and at once by a drastic purge, such as Pulv. Jalapæ 30 gr., Colocynth 10 gr., Calomel 7 gr., or Croton Oil 2 min., followed by turpentine enemata. In the hope of directly stimulating the renal secretion Pilocarpine $\frac{1}{100}$ gr. may be injected hypodermically, but pituitary extract with atropine probably produces a better result (one vaporole of extract (B. W. & Co.), and $\frac{1}{100}$ gr. atropine every four hours). For the same reason the amount of fluid in the tissues must be increased; it will be found very difficult to get the patient to take large quantities of fluid, but if possible fluids should be given as in the case of pyelitis.

One to one and a half pints of normal saline should be gradually run into the tissues every six hours. Five per cent. solution of glucose, one pint every eight hours, is a hypertonic solution, and is probably far better (the necessary quantity of glucose can be readily obtained in tabloid form and added to boiled water). The arrangement of letting the fluid run through the needle into the tissues by gravity from a Thermos flask is, I suppose, now too well known to need description. Two and a half per cent. glucose solution may be injected into a vein; but intravenous injection has no advantage over slow injection into the tissues; indeed, the latter method is in every way preferable. If the solution is not absorbed into the tissues, as shown by the disappearance of the local swelling, there is obviously no reason to repeat the injection. Surgical interference in the acute condition appears to me inadmissible, and likely only to precipitate the fatal end.

The prognosis of this terrible condition is most grave. If the kidneys can once be got to secrete freely recovery may ensue, and then the question of surgical treatment by draining the bladder or even draining the pelvis of one kidney with a large tube, if there is any reason to believe that one kidney is more affected than the other, may be considered. On the other hand once complete suppression has set in, the condition is almost hopeless.

Chronic Pyelonephritis.—This condition is most usually caused by an ascending infection from a septic bladder, and most often is the insidious early part of the disease which terminates as acute pyelonephritis. Its characteristic symptom is the presence of large amounts of pus in the urine; the urine is usually acid, but ammoniacal urine is not unknown. Bacilluria is very rare, but, of course, organisms can be cultivated from the urine, and these are usually coliform; there are often symptoms of vesical irritation.

A thick layer of creamy pus in an acid urine should at once indicate that the kidneys are probably affected. In such a case the symptoms of renal insufficiency—thirst, dry tongue and skin, chronic frontal headache, polyuria and occasional lumbar pain—should be first inquired into. Next the excretory capacity of the kidneys should be examined (see *Renal Adequacy*). If the kidneys are known to be adequate it is imperative that the cause should be attacked at once and thoroughly treated, this including a full radioscopic examination of the whole urinogenital tract, examination of the urethra and prostate, cystoscopic examination, and examination of the orifices of the ureters. It is to be remembered that the disease is almost always bilateral (85 per cent.), still proof may be obtained that it is unilateral. The cause of the septic cystitis, whether due to stone, enlarged prostate or simply coli infection, should now be dealt with, and it is probably the wisest course to drain the bladder first if there has been chronic obstruction. If the pyelonephritis is proved to be unilateral, and the remaining kidney adequate, the diseased kidney should be explored and drained. If there be stones in the pelvis or ureter these are removed and the case will probably do admirably. Pyelonephritis caused by stones in both kidneys presents a difficult problem. If the kidneys are adequate, an attempt should be made to remove the stones on what appears to be the worst side, and when this has healed

up the other side should be dealt with. If the kidneys are inadequate, on the other hand, no operative procedures on the kidneys are advisable until, if possible, their secretory power is improved.

It is imperative to insist that no medicinal treatment should be undertaken and continued in the early stages of chronic pyelonephritis in the absence of a complete examination of the urinary tract by a competent surgeon. No change in the condition can or ought to be expected from the continued empirical use of drugs unless the original cause has been found and dealt with.

As *adjuncts* to surgical treatment urotropin, tetramine, hetraline or helmitol 5 gr. every four hours may be given if the urine is acid, ammonium benzoate 10 gr. if the urine is alkaline. Simple diuretics may be given freely, the amount of fluids taken should be regularly increased so as to flush out the kidneys, and the amount of proteins taken may well be curtailed. Minute doses of calomel $\frac{1}{20}-\frac{1}{6}$ gr. three times a day for a week at a time are strongly recommended by some. The patient should be specially told to avoid the risk of a chill or a wetting, and the seriousness of his condition should be insisted on. In many cases vaccine treatment in conjunction with the rest shows good results; the vaccine should in all cases be autogenous. One to two millions should be given for the first dose and repeated in four to five days, rising rapidly from 10 to 100 millions, 150 millions may then be given for six doses with a week's interval, and then 200 millions for six to twelve doses with the same intervals. But it must be admitted such treatment is long and tedious.

One last word—Medicinal treatment of chronic pyuria without a thorough examination of the whole urinary tract by every means at the surgeon's disposal is merely trifling with human life. J. K. M.

LARDACEOUS DISEASE

The connection between lardaceous degeneration in the liver, spleen and kidneys and prolonged suppuration is well known. Treatment of suppuration should be prompt, and as soon as albuminuria is discovered in a chronic suppurating case the cause of the suppuration should, if possible, be removed.

The various forms of surgical treatment recently advocated, which vary from opening up sinuses to the removal of the entire large intestine, belong more particularly to surgery.

It is worth nothing that when suppuration has ceased the lardaceous changes disappear first in the liver, next in the spleen and, last of all, in the kidney. J. K. M.

SYPHILIS OF THE KIDNEY

"It is impossible to deny but difficult to prove the existence of chronic nephritis due to acquired syphilis."—(Herringham.)

There is a general feeling that all forms of nephritis may be met with in syphilis, but some are sceptical whether they are actually due to the spirochæte or are merely associated with the disease.

Gummatous changes independent of diffuse infiltrations are extremely rare. Old sclerotic changes in the kidney are known, but cannot be definitely proved to be due to syphilis.

Nephritis in the Secondary Period.—The kidney is affected in 3 per cent. of cases according to Petersen. An acute parenchymatous nephritis occurs which is indistinguishable from scarlatinal nephritis with one exception, that is to say, that enormous quantities of albumen may be present but the amount of urine is not lessened in the same degree as in scarlatina. The renal permeability of methylene blue is either normal or raised. During the same period it will be remembered that albuminuria in small quantities is comparatively common.

Nephritis of the Tertiary Period.—Sclero-gummatous changes may occur in gummatous kidney. There is a form closely simulating chronic Bright's disease. A case of gummata of the kidney where actual signs of a renal tumour were present has been recorded by Sir A. Bowlby, and gummata may give attacks of pain similar to that of renal calculus.

With regard to treatment, most are agreed that mercurial treatment in syphilitic albuminuria is not very satisfactory and, in some cases, appears to aggravate the condition.

On the other hand, cases have occurred lately that have been successfully treated with Neosalvarsan. J. K. M.

TUBERCLE OF THE KIDNEY

In the study of infection of the kidney with the tubercle bacillus we find endless varieties of pathological conditions varying from the most minute collections of round-cell infiltrations to extensive miliary tubercles of the renal cortex and in extreme cases we may find the whole kidney enlarged and its cortex converted into bags of caseous material from which all cellular structure has long since vanished. Our attention is naturally directed to the study of what the primary cause of the disease may be, but here again we are beset with difficulties. In a great majority of cases it may be said to be due to an ascending infection of tubercle from the bladder either by the ureters or (more probably) by the lymph vessels, and tuberculous ulcers are to be found by the

cystoscope in the neighbourhood of the ureter. Tubercle of the kidney is, as has already been pointed out, a rare cause of pyonephrosis. Two other pathological facts remain to be mastered, and these are of intense importance—

1. There is practically no evidence of healed tubercle in the kidney in post-mortem examinations.

2. The second kidney is diseased in much more than half of all cases.

Having in view these statements one cannot fail to be pessimistic in considering the treatment of renal tuberculosis. The symptoms of the disease are, it will be remembered, pyuria with some lumbar pain, and considerable symptoms of vesical irritation, whether the bladder is affected or not, together with the recognition of the presence of the tubercle bacillus in the centrifugalised urine. The irritability of the bladder in some cases is most intense.

In a case presenting these symptoms the first essential in treatment is that the locality and extent of the tuberculous infection should be accurately diagnosed.

Cystoscopy should first be carefully undertaken, and despite its difficulty every attempt possible should be made by prolonged washing out of the bladder to obtain a satisfactory view. By this examination the surgeon ought to be able to decide on the presence or absence of tubercles in the base of the bladder, and their precise locality as well as the condition of the ureteric orifices.

If (1) there are no vesical tubercles the possibility of one kidney being affected is strengthened. (2) One ureteric orifice is normal and discharging healthy urine, whereas the other is red and "pouting" and discharging pus—the diagnosis is made still more certain. (3) In such a case, if possible, the diagnosis should be further confirmed by catheterisation of the ureters.

When tubercles are found in the bladder, on the other hand, the probability that both kidneys are affected is very strong. This can be further confirmed by an examination of the ureteric orifices and by catheterisation of the ureters.

In the fortunate and exceptional cases where tubercle is definitely proved to be confined to one kidney the removal of that kidney is most strongly indicated to avoid infection of the bladder, and possibly of the other kidney. It may be noted that Hurry Fenwick long ago called attention to this particular type of case and believed it to be due to lymphatic infection from a tuberculous epididymis to the kidney of the same side "missing out" the bladder—thus the history and condition of the epididymis may well be inquired into.

Where the bladder is affected and it is doubtful whether one or both kidneys are involved, unless there is clear evidence the diagnosis should be made that both kidneys are affected, and in the writer's opinion there is no room for surgical interference with the kidneys, and treatment—other than the draining of the bladder for the local conditions there present—should be entirely medical.

We are here faced with the question of tuberculin treatment—Herringham from a very wide experience of this condition advises it in all cases except those where removal of a kidney can be undertaken. He uses 0·00001 mg. of a human bacillary emulsion for the first dose, and injects twice weekly, increasing the dose with each injection 0·00001–0·00008, 0·00008–0·0001, 0·0001–0·0002. If the temperature rises more than one degree after an injection he misses the next injection due, and then at the same interval returns to the dose which originally caused the rise of temperature—several months of this vaccine treatment are recommended. At the same time there is no doubt that it will be well to give urotropin in the hope of its bactericidal effects, while belladonna and hyoscyamus will be required to diminish the distressing spasms; buchu tea, made by infusing an ounce of the leaves for five minutes in a pint of boiling water, may be given—up to half a tumblerful twice a day. All being said I must own to a profound feeling of pessimism in this terrible disease. In the mild cases confined to one kidney all is well. In the others life is one unutterable agony, and drainage of the bladder offers the only relief—and that a temporary one—to the patient's sufferings. J. K. M.

PERINEPHRITIS AND PERINEPHRITIC ABSCESS

Suppuration in the perinephric area is usually due to extension of inflammation from a pyonephrosis. Owing to the looseness of the tissue in this region it is usually an acute process and extends rapidly. In some cases, primary inflammation takes place in this area and a certain number of acute pneumococcal abscesses have occurred in this situation.

It may be observed that the hip is usually flexed, as is also the trunk towards the affected side and also that pain is complained of in the knee. In the point of view of diagnosis, these symptoms should be remembered.

Treatment consists in free exploration and drainage. In the acute stage belladonna and laudanum stupes with aspirin internally to relieve the pain. J. K. M.

HÆMATONEPHROSIS

This condition is very rare. It may be described as being the distension of the kidney

with blood, the cause being rupture of some main artery, usually near the pelvis. Aneurysm of one of the branches of the renal artery has been described as a cause. The possibility of this as an acute condition should be remembered.

In a case of the author's, a man was admitted to hospital cold and pulseless, complaining of pain in one loin. This condition of profound shock lasted for a day, and shortly after this a large renal tumour was discovered in the loin.

Skiagraphs showed a doubtful shadow in the ureter and, not unnaturally, the condition was diagnosed as one of hydronephrosis owing to the ureter being blocked by a calculus.

When the shock had completely passed off, the kidney was exposed and fortunately a semi-fluid tumour was first tapped with a small aspirating needle and pure blood drawn off; no stone was found in the ureter.

The opening of the kidney was secured and, at a later date, when coagulation was complete, the kidney was removed.

The case is worth attention for the preliminary aspiration and recognition of the case had not a little to do with the patient's recovery.

There was no hæmaturia in this case, but in a similar case recorded by Herringham there was profuse hæmaturia. J. K. M.

RENAL CALCULI

Renal calculi may be composed of oxalates, urates, uric acid, phosphates, cystin or of mixtures of these. It is necessary to consider some of the factors in the production of such calculi before discussing their rational treatment. The importance of infection as a factor in starting the aggregation of crystals into a calculus is well illustrated by the case of cystin stones. Cystinuria depends on a congenital metabolic defect in the breakdown of the sulphur-containing amino-acids of the tissues. In a family of cystinurics described by Garrod, only one member developed a stone and that one had bacilluria. In the treatment of any form of calculus, therefore, every effort must be made to render the urine aseptic by the methods described under pyelitis. (See also article on *Urinary Antiseptics*.) The only other suggestion as to prophylaxis against cystin calculi that has been made is based on the hypothesis that this endogenous cystin should become the taurin of the bile salts, and that its excretion as cystin is due to lack of cholalic acid with which it can conjugate. Cholalic acid may, therefore, help in preventing cystinuria. It can be given as tablets of colalin $\frac{1}{8}$ gr. to $\frac{1}{2}$ gr. three times daily before food. Restriction of the sulphur in the food has no effect, as this can be metabolised satisfactorily by the body. Alkalis help to dissolve cystin stones when formed, but cannot check the formation of fresh stones.

Benjamin Moore has shown that even in a uric acid stone the core is most frequently composed of calcium oxalate with some colloidal substance, possibly blood. In the prophylactic treatment of calculi it is therefore important to avoid oxaluria, as it may cause hæmaturia and thus provide a colloidal binding for a stone. Oxaluria may result from—

(1) Ingestion of food rich in oxalates, such as rhubarb, strawberries and spinach. It is doubtful whether any other article of food contains oxalates in sufficient quantity to produce symptoms. (2) From gastric or intestinal fermentation. This appears to take place under two opposite conditions of gastric secretion. If there is insufficient hydrochloric acid in the stomach, fermentation of the carbohydrates will occur there with the resulting formation of oxalates. If, on the other hand, there is hyperchlorhydria, it will probably be found, as pointed out by Mayo Robson and Cammidge, that oxaluria is associated with chronic pancreatitis. For the treatment of this condition see the article on *Diseases of the Pancreas*. It will follow, therefore, that in any case of oxaluria, careful attention must be paid to the state of the digestion. (3) In neurasthenic conditions, when oxaluria may occur in crises. At present, the method of production of the oxaluria in these cases is not understood, but treatment must be directed towards the nervous system.

Should deposit of oxalates occur, the recognised treatment is abstention from oxalate-containing foods and administration of magnesia, since the oxalates are more soluble in its presence. It has been shown that when the amount of CaO and MgO in the urine are about equal calcium oxalate remains in solution—probably owing to a formation of a soluble double salt. Peas should be taken when in season, as they are poor in oxalates and rich in magnesia. Potassium citrate is of service in two ways: (1) As a diuretic, diluting the urine; (2) by combining with the calcium it prevents the formation of calcium oxalate crystals. C. J. Martin showed that citrates form a non-ionisable double salt with calcium. Some observers prefer to employ lemon juice to sodium or potassium citrate. The drinking of lemon squash will tend to prevent oxaluria from eating strawberries.

An increase in urinary acidity will assist the solution of an oxalate calculus when it has once been formed, but the difficulty is that such increased acidity will promote deposit of uric acid crystals round it. Nevertheless R. Maguire has found that the administration of acid sodium phosphate (NaH_2PO_4) in doses of up to 1 oz. a day in 100 oz. of distilled water is effective in

diminishing the size of oxalate calculi. It is obviously important that there should be no ingestion of oxalates during this treatment, as the acid salt would facilitate their absorption.

The principal factors in the deposit of uric acid crystals in the urine is high acidity and high percentage. Acidity is at its height during fasting hours and is seldom a marked feature during digestion owing to the secretion of acid into the stomach. It is usually sufficient to give 20 grs. of potassium citrate night and morning to correct high acidity. There is one precaution which seems to me very important. If uric acid deposit has already occurred in the form of a calculus, rendering the urine alkaline would cause growth of the calculus by accretion of phosphates. The patient should, therefore, be told to put a piece of red litmus paper into the morning urine. If it turns blue, the drug must be diminished in amount until this just fails to occur. Fresh fruit such as pears, green figs, dates, oranges and grapes have a similar action in checking high acidity.

High percentage of uric acid may be absolute or relative, that is, the total output may be increased or the urine may be concentrated. Either would favour deposition. The former should be regulated by cutting off food rich in purins (see article on *Gout*), the latter by diluting the urine. Patients do not usually care to be ordered to drink plain water. Potash water is preferable to soda water because of the relative insolubility of the sodium salt. Lithia water formerly had a great reputation as a solvent of uric acid, but it is certain that it is ineffectual in the doses ordinarily taken, and that if sufficient lithia could be absorbed to be an effective solvent it would be poisonous. Really, it is the water which is the chief therapeutic agent. Certain waters such as those of Contrexéville have a high repute for washing out uric acid. It has been questioned, however, whether the treatment of Contrexéville does not increase the endogenous formation of uric acid; whether, in short, as Goodhart says, the gravel passed is not manufactured on the premises. But an alkaline mineral water will help to prevent deposit of gravel both by diluting the urine and by rendering it less acid. Few things are better than Evian water for this purpose.

Gee pointed out the extraordinary effect of whey in preventing uric acid deposits, and I can confirm this. It is not clear whether the effect is due to its diuretic action, but there is no doubt as to the fact. A breakfast cupful should be given twice or thrice a day.

Atophan is distinctly contra-indicated in uric acid gravel or calculi, because of its marked effect in increasing the output of uric acid.

Phosphates are always secondary in calculi, being deposited around some other substance and never forming the core. Normally phosphates are present in the urine as (1) acid phosphates of sodium and potassium; (2) earthy phosphates of calcium and magnesium. It is only the earthy phosphates which can form a deposit. The appearance of "knife rest" or "coffin-lid" crystals of ammonio-magnesium phosphate ("triple phosphate") is definite evidence of ammoniacal decomposition, probably due to a streptococcal or staphylococcal infection (for the treatment of this complication see *Pyelitis*). Apart from triple phosphates a phosphatic deposit is practically always due to diminished acidity of the urine and seldom to an absolute increase in the excretion of phosphates. If the urine is rendered acid, the deposit of phosphates will cease. Nitro-hydrochloric acid may be given for this purpose, and once the urine is made acid in this way it may be kept so by giving acid sodium phosphate in 30 gr. doses three times a day.

Sorebeer's diet has been tried in phosphaturia. Milk, eggs, fish and fruit, which contain a good deal of lime, are not allowed, while foods poor in lime, such as meat, potatoes and cereals are given. The phosphates are then excreted in a more soluble form. But as the phosphatic deposit depends either on ammoniacal decomposition or simple reduction of acidity, rather than on an absolute increase in the excretion of phosphates I have not tried it.

Renal calculi may produce both mechanical and septic results calling for treatment. In the former group are chronic renal pain with attacks of hæmaturia, renal colic and hydronephrosis; in the latter pyelitis, pyelonephritis, pyonephrosis and perinephric abscess. Only the first two come within the scope of this article.

Renal Pain.—If a renal calculus is diagnosed and this is confirmed by the X-rays, operative removal is indicated. The pain may be referred to the side opposite to that which contains the stone, so a skiagram must be taken of both kidneys. If the diagnosis is uncertain or operation is refused or postponed, the urine must be carefully examined for crystals and the treatment appropriate to the deposit continued as described under prophylaxis. A quiet life is advisable; horse exercise, railway journeys and violent exertion are well known to excite an attack of renal colic by starting the stone on its way down the ureter. For the symptomatic relief of pain, aspirin in 10 to 15 gr. doses, hot baths or antiphlogistine to the loins may be of service. Morphine should naturally be avoided in the treatment of chronic renal pain, on account of the danger of establishing a habit.

Renal Colic.—In the attack nothing is better than morphine tartrate $\frac{1}{6}-\frac{1}{4}$ gr. together with

atropine sulphate $\frac{1}{100}$ gr. hypodermically. The antispasmodic effect of the atropin aids the anodyne action of the morphine, and aids the onward passage of the stone. With morphine alone there is apt to be recurrence of the pain as the anodyne effect passes off. Tincture of belladonna 10 min. in 1 oz. of water should be given by the mouth every three or four hours until the pupils are dilated, the face flushed and the mouth dry. I have seen quite fair-sized stones passed *per vias naturales* under this treatment. Inhalations of chloroform may be necessary at the outset until the drugs have had time to act. Hot applications to the loins or the hot bath may help to relax the spasm. When under the influence of the atropin, barley water, lemonade or Evian water may be drunk freely to try and wash the stone along. Inversion of the patient is advised and a change of posture may certainly help to disengage the stone from the ureter. After the paroxysm is over the aid of the X-rays should again be invoked to locate the stone. W. L. B.

DISEASES OF THE PROSTATE

Acute Prostatitis.—This is usually met with in the second or third week of an acute gonorrhœa, though it may arise *de novo* as a result of a Bacillus coli septicæmia.

Fever is present and the prostate can be felt from the rectum swollen, hot and tender. After about three weeks the acute stage subsides and resolution occurs or the disease becomes chronic.

The patient should be persuaded to keep his bed, which he will usually do if there is much fever or if epididymitis is also present. Confinement to bed turns the scale in favour of the patient's bactericidal powers, and cannot be too strongly insisted upon. Prescribe diluent drinks and a non-irritating diet and prohibit alcohol. Local treatment must be of the gentlest description and consists of—

1. Antiseptic washes or injections for the *anterior* urethra only, such as potassium permanganate 1 in 3000 or albargin 1 in 2000.
2. The application of local heat by means of hot baths, hot-water bottles, fomentations.
3. Rectal suppositories containing iodex are of considerable value.

In very acute cases there will be complete retention of urine. If this will not yield to hot baths and a draught of 30 min. of laudanum a catheter should be passed as often as required. There need be no fear of infecting the bladder with the gonococcus by this procedure, which is preferable to suprapubic puncture.

The most serviceable drugs are those which relieve the pain and cause diaphoresis, aspirin being about the best. In severe cases morphia may be required. If chordée is very severe prescribe a bromide mixture, but in milder cases the chordée is at once relieved if the patient rises and passes water. If there is dysuria the best drug is some preparation of sandal oil.

Chronic Prostatitis.—This is usually the result of an acute prostatitis of venereal origin, but may be a very troublesome complaint of non-venereal hæmatogenous origin (Bacillus coli, streptococcus, staphylococcus), in those who ride or motor to excess or indulge in prolonged or too frequent sexual excitement.

The symptoms are protean and include intermittent gleet, the passage of threads in the urine, urethral irritation; pain in the urethra, perineum, rectum and back; sexual neurasthenia and impotence; chronic arthritis, lumbago and sciatica. It is surprising in how many cases of chronic joint trouble the source can be tracked to a latent bacterial focus in the prostate gland, and how quickly such disabling complaints melt away under suitable treatment applied to the organ.

The diagnosis can only be made by placing a finger in the rectum and squeezing out a drop of prostatic fluid, placing it under the microscope and detecting *pus cells* and *bacteria*.

It is one of the commonest diseases of modern life and tends to persist indefinitely unless treated on modern lines, and yet it is seldom recognised, as the method of diagnosis is not widely known.

The patient must get about and try and "keep fit," he should sleep in country air, feed up, take regular and sufficient exercise and school himself not to worry about his condition—a task in which he can and should be constantly and wisely aided by his doctor.

Great patience is required on the part of both, and it is well to start by naming three months as the earliest time for the duration of treatment.

The patient must be careful not to over-exercise or overwork till exhausted, as this allows the disease to take fresh hold, and no horse-riding, bicycling or long motor rides must be permitted, as constant bumping of the prostate is most harmful. No sexual excitement of any kind is to be permitted, as it at once sets back the favourable progress of treatment.

The patient will often complain of nocturnal pollutions. These can do nothing but good, as by this means the prostate is emptied of its contents with very little accompanying hyperæmia.

Not a drop of alcohol must pass the patient's lips till he is cured. Even a single glass of wine is often enough to cause a recrudescence of urethral discharge and to set back the clock of the disease for weeks.

The key to successful treatment is prostatic massage. If the disease is left to itself it takes years to die out and may persist indefinitely. The gland and its ducts become clogged with inflammatory products and no progress is possible. It is proved by experience that if the gland can only be emptied at regular intervals and without the hyperæmia attendant on sexual excitement the clogged ducts are cleared, the acini emptied of pus, fresh serum is poured out into the acini charged with bactericidal substances, the circulation of lymph is favoured whereby noxious products are carried away and the gland slowly but surely returns to the normal state.

After all the best antiseptic wash we know is healthy tissue fluid, and by this simple means we can secure that the whole gland is washed out with this fluid at regular intervals.

It is found by experience that massage should not be performed too often. Every fourth to seventh day is quite sufficient to secure a good result. It is also important not to persist too long with any given course. Four to six weeks should be the limit. At the end of that time all treatment should be put aside for at least three weeks and the patient should be persuaded to take a short holiday in sea air, either on board ship or playing golf at the seaside. Many a patient sent away like this with a fair amount of pus still present in his secretion returns without a trace of it and absolutely cured.

If this happy result is not attained a further course of massage should be instituted, and in nineteen cases out of twenty a perfect cure will in time be attained. In those cases which fail to clear up after some months it is as well to seek special advice.

The process of massage is very simple and only takes a few minutes. By means of a gloved finger inserted into the rectum of the kneeling patient the operator makes *gentle* pressure against the anterior wall of the rectum. The finger is made to work from without inwards and downwards towards the middle line over the back of the vesicles and prostate. In a minute or so a bead of secretion appears at the meatus and this is the signal that enough has been done. *No force must be used or the wall of the rectum may be torn.* Peaceful persuasion is here the motto. The patient then passes water and thereby washes out the urethra. An instillation should now be made into the deep urethra. This is done with an "Ultzmann" catheter and syringe which can be obtained from any instrument maker. The best solution is 5 gr. of silver nitrate in 1 oz. of distilled water, 1 dr. of which is used for each instillation.

There are no specific drugs for this complaint, but it is important to prescribe tonics, especially nux vomica and strychnine, which help to raise the tone of the prostatic musculature and brace the patient's nervous system and keep him from worrying.

New Growths of the Prostate.—These are simple fibro-adenoma (90 per cent.) and carcinoma (10 per cent.). They are seldom met with under the age of fifty. The early symptoms are increased frequency of and difficulty in micturition and hæmaturia. The second stage is marked by attacks of acute painful retention. In the last stage appears the giant toneless painless bladder that overflows every few minutes. The diagnosis is made by rectal examination and *by cystoscopy*.

The treatment may be symptomatic or curative by removal of the cause.

Symptomatic. General Treatment.—Most of these patients will be found to have a high blood pressure, and this should always be measured. If found excessive the general directions for those with high blood pressure must then be reviewed for the patient's benefit. "Moderation in all things" is the motto. No rushing to catch a train, no straining at stool, no straining to pass water, and moderation in the sexual life. There is great risk from a sudden exposure to chill, so that careful attention must be directed to questions of climate, dwelling-house, ventilation, bathing, bed-clothes and dress. The attacks of acute painful retention are brought on by anything that drives the blood away from the surface and produces congestion of the portal and pelvic veins. Such things are chill, constipation and heavy meals.

A moderate, light, mixed diet is therefore to be prescribed, and only the lighter forms of alcohol should be taken, and those in small amounts. So long as there is no unrelieved obstruction a glass of diuretic table water such as Evian, Vichy or Contrexeville should be drunk on an empty stomach, morning and evening, with the object of flushing the kidney tubules. As regards drugs, remarkable amelioration of the symptoms can usually be secured for some years by their use.

In this connection I have found the best mixture to be one containing 3 gr. of urotropin and 20 gr. of acid sodium phosphate. If this fails to relieve the symptoms nux vomica or ergot will often succeed, and nitric acid and phosphoric acid may also be worth a trial.

Symptomatic treatment includes the use of the catheter. The catheter should be used if there is an attack of complete painful retention, but only after the patient has been given a hot bath and has been put to bed in blankets, during which time the doctor can have made all his preparations to pass a catheter with aseptic ritual. The best catheter is a No. 10 English

scale black or yellow gum-elastic, called "the Marshall," supplied by Bell and Croyden. The best lubricants are "catheter purin" or the "K-Y lubricant" which can be obtained in tubes. Draw off 20 oz. of water every four hours until the bladder is empty, by which time the patient will usually be able to pass water again naturally.

If the frequency at night is so great as seriously to disturb the patient's sleep, it may be necessary to pass a catheter last thing at night, but such patients would be far better advised to undergo an operation. I never prescribe catheter life unless—

1. The kidneys are so far gone that an operation is inadvisable, the patient being unable to micturate at all, or the bladder filling up so quickly owing to polyuria that it needs relief every few hours.

2. The patient refuses operation and there is enough residual urine for the bladder to be palpable above the pubes, or there is chronic cystitis which requires lavage.

In the ordinary cases with only a small amount of residual urine I am of opinion that the patient, if he refuses operation, is far more comfortable and runs less risk if he has no catheter treatment. The profession have been far too ready in the past to have resort to the catheter. The mortality from the catheter is greater than that from operation. The catheter should never be used for *diagnosis* of the amount of residual urine.

3. As a preliminary course for patients with partial renal failure so as to relieve the kidneys of their load and put them in a fit state to withstand an operation.

Curative Treatment.—Modern medicine endeavours to replace symptomatic treatment by treatment based on knowledge of pathology and aims at removing the cause of a disease. Modern surgery may be said to have conquered most of the difficulties that surround the removal of the cause when Freyer can publish a series of 1,036 cases with 57 deaths, and Young can publish a series of 450 cases with 17 deaths. These results can, of course, only be obtained by those who practise the operation assiduously.

I have recently published (*American Journal of Dermatology* August 1912) a consecutive series of cases of my own operations performed half under stovaine spinal anæsthesia and half under general anæsthesia on patients as they came up to a large general hospital in all stages of the complaint, no case being refused operation, no preliminary treatment being employed. By this means I was able to prove that cases of adenoma of the prostate can be divided into three groups as regards operative mortality.

The first group includes those who complain of irritability of the bladder with or without attacks of painful retention of urine, but who show no signs of renal failure (functional tests)

In this group the mortality was nil.

The second group includes cases with similar symptoms, but who also show signs of renal failure. In this group the mortality was nil when stovaine spinal anæsthesia was used, but was higher when chloroform was used.

The third group is distinguished from the others by the fact that the patients complain of passing water every few minutes and on examination is found a painless atonic distended bladder extending to the umbilicus. In this group the mortality was very high whichever anæsthetic was used.

These facts show the extreme importance of knowing how to select the right cases for operation if the mortality is to be nil or almost nil. The mortality in the last two groups might seem at first sight too high to justify operation at all, but by recent work I have now satisfied myself that even in these groups the mortality can be reduced to a low figure *if three months preliminary treatment is employed of regular catheterisation*, copious drinking and administration of urotropin, or, better still, permanent drainage by suprapubic cystotomy.

There is, therefore, no need to refuse operation flatly to patients within these latter two groups, but it must be refused unless preliminary treatment has been carried out for three months or longer until the functional tests show that the kidneys have recovered their power. (The functional tests cannot be described in this article.)

These facts also indicate the necessity of urging operation during the first few years of the complaint, when the operation is not dangerous and a complete cure can be promised.

It is not fair to treat these patients symptomatically for years until their bladders and kidneys are worn out and then expect the surgeon to operate on them when the proper time for the operation is passed.

Summary.—Catheter life never cures, it only relieves symptoms, it is far more dangerous than most people realise and it is the source of much worry and loss of time. In its favour can be urged that it seems a far less dangerous step to the patient and his friends, and these considerations may be allowed due weight when the patient can afford the time and care required to carry out the catheter ritual.

Three months' course of catheter life or drainage by suprapubic cystotomy should always be prescribed before proceeding to operation in those whose kidneys show definite signs of diminished power. On the other hand, operation seems a big step to take and presents a certain amount of immediate risk and acute discomfort; but in its favour can be urged that the risk is

smaller the earlier the patient presents himself for operation, and that three months after the operation the patient will find himself cured of his obstruction for good and all. That is to say, he will never need the catheter again, the stream will be free, the urine will be clear, the frequency will be normal and the kidneys will be saved from slow death by back pressure and infection. The warmest advocates for the operation are those who have passed through it themselves.

At the same time it is well to remember that good results can only be obtained by those who practise the operation constantly. Only by this means is it possible to ensure that the diseased gland is delivered cleanly and quickly; that the patients are selected wisely; and most important of all that all those minute details in the after-treatment be attended to which do so much to put the finish on a successful operative removal. F. K.

INFLAMMATION OF THE BLADDER

A patient suffering from cystitis complains of pain in the bladder region and at the end of the penis, increased frequency of micturition and the passage of pus and blood. It is a common mistake to make a diagnosis of *cystitis* when, as a matter of fact, the patient is suffering either from *pyelitis* or *prostatitis*. In these two conditions cystitis, if present, is only a minor incident.

If fever is present the case cannot be one of pure cystitis. Fever with pyuria in a woman is always pyelitis, and in a man is usually prostatitis. This is a most useful diagnostic rule. The diagnosis of cystitis from pyelitis can be made in the following manner. The urine should be passed into two glasses. If the second is cloudy the case may be either cystitis or pyelitis. If there is fever it must be pyelitis.

If there is no fever the diagnosis can only be made by cystoscopy and catheterisation of the ureters. In some cases there may be a large tender kidney, which renders the diagnosis easy, but in other cases there may be no symptoms pointing to the kidney. In the male the diagnosis of cystitis has also to be made from posterior urethritis and prostatitis. The patient is asked to urinate into two glasses; if the second is clear the case cannot be one of cystitis, and the pus must be coming from the urethra. The contents of the prostrate gland are then expressed by means of gentle pressure of a gloved finger inserted into the rectum. A drop of the secretion is caught on a slide and should be examined under a microscope, and of another drop a culture is made. Microscopic examination shows the presence of pus cells and bacteria. The culture reveals the nature of the bacteria. It cannot be too often emphasised that most male patients with fever, rigors and pyuria are cases of prostatitis. Such a prostatitis may be secondary to gonorrhœa, but is very often a spontaneous infection with the colon bacillus.

Pyelitis and prostatitis having been excluded, a diagnosis of cystitis is not yet sufficient. In the first place it is necessary to determine the exciting cause, namely, the organism by means of film preparations, cultures and inoculation experiment in order to determine if it be the tubercle bacillus, the colon bacillus, the gonococcus, a streptococcus, a staphylococcus or a proteus. These are the only bacteria that commonly infect the urinary tract. (At this point it is well to state that if the tubercle bacillus is found the primary focus must be either in the testis or the kidney. Primary tuberculous cystitis is unknown.)

Having determined the bacteria present, the practitioner must not rest content, but must proceed to find out finally whether there are any predisposing causes present. It is not uncommon to meet with patients at the present day who have been treated for months with emulsions of bacteria isolated from purulent urine with no improvement ("vaccine" treatment). When these cases come to be examined in a proper manner the reason becomes clear, usually a stricture is present, or an enlarged prostate or a stone. Naturally such cases will not clear up until these predisposing causes have received proper surgical attention. The common predisposing causes of cystitis are as follows: Stricture and enlarged prostate, stone, tumour, diseases of the nervous system and the passage of unclean instruments. Uncommon causes are: foreign bodies, parasites, pouches. Until all these have been excluded it cannot be said that the case has been properly examined.

When the diagnosis has been rendered complete the practitioner can proceed to the consideration of the treatment. If a predisposing cause is present it should be removed whenever feasible, the cystitis will then usually clear up forthwith in a few weeks. On the other hand, no predisposing cause may be found. A certain number of cases of hæmatogenous spontaneous cases of cystitis are met with, especially in young males. The onset is usually acute, with considerable hæmorrhage, though it may be insidious and with slight hæmorrhage, the organism concerned being usually the proteus. If the bladder is inspected with the cystoscope ulceration is usually present, and the inflammation may be found to be confined to the bladder only. Such cases tend to clear up spontaneously in three to four weeks' time, though a few become chronic. There need, therefore, be no surprise if there is failure to find a predisposing cause.

Treatment of Acute Cystitis.—No lavage or instrumentation should be employed at the outset when the symptoms are acute. Resort must be had to general measure. Rest in bed, the application of heat by means of hot-water bottles, poultices, hot enemata and hot hip-baths will be found of great service, and the application of half a dozen leeches to the perineum brings relief. The patient should drink large quantities of fluid, as the more dilute the urine the less will it irritate the inflamed bladder. The diet should consist of milk only, and alcohol should be strictly forbidden. Sedatives will be needed, and are best applied in the form of suppositories, the most satisfactory being one that contains 1½ gr. of the extract of belladonna, 20 gr. of antipyrin, and 14 gr. of the oil of theobroma. If this fails to control the pain morphia or laudanum is required.

During the acute stage there should be no thought of trying to kill the bacteria by means of drugs. The indication is to render the urine as little irritating to the bladder as possible, and leave the killing of bacteria to the natural antiseptics contained in the inflammatory exudate. Acid urine is more irritating than alkaline urine, so that the wise course is to give alkalies. A good mixture contains 20 gr. of potassium citrate, 20 min. of the tincture of hyoscyamus, 10 min. of the emulsion of chloroform, and is made up to the ounce with the infusion of uva ursi. It may be given every four to six hours. In a few days the symptom should subside under this régime, and the case may clear up entirely by natural repair, or it may become chronic.

In the treatment of chronic cystitis it is of the utmost importance to attend to the general health. The patient must be warmly clad, and, if possible, should be removed to a warm seaside place on the south coast. He should be encouraged to live in the fresh air and to take plenty of good food, aided thereto by an appetising tonic. He should drink at least four pints of fluid in the twenty-four hours, and more if he can manage it—preferably Contrexéville, Evian, or Vichy water, and only the mildest forms of exercise should be permitted.

In the treatment of chronic cystitis two further principles are employed, namely, lavage and the administration of urinary antiseptics.

1. **Lavage.**—Lavage is especially indicated for cases with ammoniacal urine. The urine is rendered ammoniacal by the presence of certain bacteria, usually the proteus or a staphylococcus which can split the urea into ammonium carbonate and ammonia. It is very difficult to kill these bacteria by means of urinary antiseptics taken through the mouth. The indication is to diminish the bacteria by lavage, when it may be possible to restore the acid reaction of the urine and then obtain the full effects of urinary antiseptics. In ammoniacal cases, while lavage is being carried on, the following mixture should be given, for reasons which will be explained later: boric acid 15 gr., ammonium benzoate 15 gr., emulsion of chloroform 10 min., infusion of uva ursi to the ounce. Lavage should be carried out twice a day if the bladder is not too irritable. If the washings are found to irritate they should be carried out once a day, or even less often, until the bladder becomes more tolerant. The best method for washing the bladder is the method of Janet, by means of hydrostatic pressure. It is the best method because no catheter is required. The apparatus needed can be obtained from Montague, of 69 New Bond Street, and is known as the author's outfit. It consists of an india-rubber bag to hold two pints of fluid, which can be hung on a nail in the wall at a height of five feet above the patient's abdomen. To the bag are attached six feet of rubber tubing and a glass nozzle. The bag having been filled with lotion the fluid is made to run, by the force of gravity, into the urethra through the sphincter of the bladder into the bladder itself. The patient soon learns to take the fluid into the bladder, and after a few minutes he passes it out again naturally.

The other method of lavage is to pass a catheter and wash out the bladder either with a syringe or with the irrigating bag. This method must always be used in the female, but should only be used in the male if there is some additional reason for passing a catheter, such as an enlarged prostate.

When the bladder has been rendered tolerant with simple washings a complete and rapid cure can often be obtained by means of instillations into the bladder of 30 min. of strong silver nitrate solution, beginning at 5 gr. to the oz. and working up to 20 gr. to the oz. These instillations are introduced by means of "Ultzmann's instillator." A lubricant is needed, and the best is the "K.Y." lubricant. In obstinate cases which fail to react to these methods a cure can sometimes be obtained by means of suprapubic drainage for a few weeks, which acts by giving the bladder complete rest.

For lavage the following solutions may be employed: silver nitrate in strengths running from $\frac{1}{10,000}$ up to $\frac{1}{1000}$ in ordinary tap water. Oxycyanide of mercury in strengths of $\frac{1}{4000}$ up to $\frac{1}{2000}$. Zinc permanganate $\frac{1}{4000}$.

In obstinate cases I have obtained remarkable cures with "gomenol," a patent preparation made up by Prevet of Paris. Forty min. of gomenol are added to two pints of warm water and thoroughly shaken up in a bottle, the resulting emulsion being used as a wash. If the case is not doing well on one kind of solution it will often react if a trial be made of others,

though it is impossible to predict in any particular case which particular solution is going to give a favourable result.

Urinary Antiseptics.—A good deal of work, from the clinical standpoint, has been carried out recently on urinary antiseptics, especially by Anson Jordan and Thomson Walker.

1. In acute cases it is not wise to exhibit drugs that act only in an acid medium. In such cases potassium citrate is the drug which relieves the symptoms, though it does nothing to diminish the bacteria. It is best made up with the infusion of uva ursi, which exercises a sedative effect and has a distinct antiseptic action even in alkaline urines.

2. In chronic cases, if the urine is ammoniacal or alkaline, it is not the slightest use exhibiting urotropin and allied drugs. This class of compounds act by producing formaldehyde in the presence of acid urine, but they are quite unable to do so in an alkaline urine. The antiseptic action is entirely due to the formaldehyde. In alkaline urine, therefore, lavage is the most important method for eliminating bacteria. Drugs that are bactericidal in alkaline urine are boric acid and uva ursi. Boric acid appears to be the most valuable drug of all, and should be given in doses of 15 to 25 gr. four times a day. Ammonium benzoate renders the urine less alkaline and should be exhibited as an adjuvant.

If the alkalising bacterium is a staphylococcus it is an indication to use sandal-wood oil, as sandal-wood oil appears to be highly bactericidal to staphylococci, but even in cases of alkaline cystitis due to other bacteria sandal-wood oil often has a most soothing influence, and will be found to be of great value as regards the symptoms. It is best given as an emulsion made up with Tr. of Quillaia or mucilage, in doses of 5–15 min. four times a day. In certain persons it causes backache or stomach ache, and must then be discontinued. It has no real bactericidal effect on gonococci.

3. If by such means the urine can be turned faintly acid, and anyhow in chronic cases with acid urine, then is the time to exhibit urotropin. Urotropin seems to be the most powerful bactericidal agent that can be given by the mouth, but can act only in acid urines. The more highly acid the urine the higher the concentration of formaldehyde, and, therefore, the better the result. In addition to urotropin drugs should be given which increase the acidity of the urine. The best of these is acid sodium phosphate, in doses of 30 grains four times a day.

4. Certain practical points must be mentioned with regard to "urotropin." Urotropin decomposes very quickly in a mixture, and should, therefore, only be given in tabloid form. These tabloids are to be dissolved in water by the patient. Urotropin can be given in larger doses than has hitherto been given. In obstinate cases it is possible to administer 20 gr. four times a day, but in most cases a sufficient dose will be 3, 5, 7½ or 10 gr. Urotropin should be given at least six-hourly, as the major part of the drug is secreted during that time. Certain patients will not tolerate urotropin. Even the minutest trace of formaldehyde in the urine in such patients may cause a most intense irritation of the bladder. It is also stated that certain persons cannot change urotropin into formaldehyde, and this may be why it fails to act in some cases. Finally in a few persons urotropin will be found to irritate the stomach, and here again it must be discontinued. It is no use giving urotropin with alkalies, and that is why urotropin is superior to any of the patent combinations of hexa-methylene-tetramine in combination with citrates, etc. If urotropin is not tolerated it is better to make use of boric acid and the benzoates, or of sandal-wood oil. Salol has been lauded in doses of 20 gr., especially by Rovsing, but in other hands it has been found disappointing as a urinary antiseptic.

5. The following points will be found to bear on the subject under consideration. However acid or however alkaline the urine is made no effect is produced on the growth of colon bacilli. All the same, during acute B. coli infections, alkalies do relieve the symptoms, and during the chronic stages acids help by increasing the action of urotropin, which does inhibit the growth of colon bacilli. The best drug for rendering the urine alkaline is potassium citrate. The best drug for rendering the urine more acid, if it is already acid, is acid sodium phosphate; but when the urine has been rendered alkaline by bacteria the best drugs to turn it acid are boric acid and ammonium benzoate.

6. Finally a few words should be written on the treatment by vaccines. In a case of tuberculous cystitis, tuberculin will only cure if the cystitis is secondary to a tuberculous testis, and in such case the cure will usually be obtained rapidly. If, on the other hand, there is no tuberculous nodule in the testis, and, of course, in all cases in females, then there is always a primary tuberculous infection of one kidney, and a cure is absolutely impossible unless the affected kidney be removed. When that is done tuberculin rapidly clears the cystitis, but if that is not done the condition may seem to improve for a time, but will eventually relapse and lead to the death of the patient. In the case of infection with the colon bacillus autogenous vaccine will often relieve the symptoms, but they will not rid the urine of bacteria. To attain this end the predisposing causes must receive attention, urinary antiseptics must be

given, and the bladder must be treated by lavage, when a cure can usually be obtained.

Other diseases of the bladder are calculus, neoplasm and parasites. Apart from associated cystitis their treatment is carried out by cystoscopy and surgical manipulations, and cannot, therefore, be considered here.

During the course of certain diseases of the nervous system, and also in the course of certain febrile and asthenic states, retention of urine may occur, and need for its relief the passage of a catheter. The precautions in vogue to ensure surgical cleanliness in catheterisation are not nearly stringent enough if cystitis is to be avoided. It has, therefore, been thought well to insert in this place directions for the passage of a catheter which do satisfy the canons of aseptic surgery and are found in practice to prevent effectually infection of the bladder. Though the description may seem a little prolix the time actually consumed in carrying out the manipulations is not long when all the apparatus required has been assembled, and the practitioner is accustomed to their routine use. It is not right to pass catheters in a light-hearted manner, as if they were simple and safe instruments. They are safe instruments if properly used, but their use is never simple, and requires religious attention to the details of aseptic ritual.

The outfit needed must include the following articles, and can be obtained from Montague & Co., 69 New Bond Street: (1) A douche tin or india-rubber douche bag to hold two pints; (2) six feet of rubber tubing and a clip; (3) a tin jug in which to make up a wash; (4) material for making up an antiseptic wash; (5) a urethral nozzle of some kind; (6) a sterile lubricant; (7) a suitable catheter; (8) some arrangement for sterilising the catheter.

The best lubricant is made up as follows—glycerine 20 parts, tragacanth 2 parts, oxycyanide of mercury $\frac{1}{4}$ part, sterilised distilled water 100 parts. This is put up in ordinary tin squeeze tubes, and is easily carried about and always ready for use. It can be bought ready made as the "K.Y. lubricant."

A No. 9 or 10 (English scale) gum elastic coudé is a good form of catheter, but perhaps the best of all is the "Marshall," made by Bell and Croyden, with a hard olivary tip, a flexible shaft and a large eye. The latter can be boiled many times, and indeed most of the best instrument makers now turn out gum elastic catheters that can be boiled. Porgés white gum elastic is as good as any of them.

After a catheter has been mechanically cleaned, boiled and dried it is best put away in a "paraform" steriliser. A catheter can be carried about anywhere in this, where it lies constantly in dry formalin vapour. In emergency work the practitioner is advised always to boil his catheter just before use. Better to spoil many catheters than to spoil one patient. An outfit for catheterisation of prostatic cases (known as the author's Prostatic outfit) is kept ready for use by Montague.

The normal urethra swarms with bacteria in its first three inches, but higher up it is sterile. The urethra must, therefore, be washed out before a catheter is passed. The best antiseptic wash for this purpose is oxycyanide of mercury, one part in four thousand of warm water. This drug may be obtained in tabloid form. If it is not to hand a 15 gr. tabloid of chinosol dissolved in a quart of warm water makes an efficient and non-irritating wash, as does a solution of lysol, $\frac{1}{2}$ dr. to a quart.

The douche bag or tin is filled with two pints of wash and suspended by a nail or held by an assistant some two or three feet above the level of the patient's penis as he lies in bed. Clipping the rubber tubing with the first finger and thumb just above the urethral nozzle which is attached to the end of the tubing, the practitioner places the nozzle just inside the urethra and allows a gentle stream to flow into the urethra and back again around the nozzle into a receptacle placed beneath the penis. The urethra, as far as the compressor urethræ, is in this way flushed with a pint or more of the wash, and is rendered sterile for the time being.

Having washed his hands in an antiseptic lotion the practitioner takes the catheter and passes it into the bladder. If the bladder is over full not more than twenty ounces of urine should be withdrawn, as if the bladder is completely emptied the sudden relief of pressure may act adversely in two ways. First, the splanchnic veins may fill up with blood, and the heart, being deprived of sufficient blood, may fail. Secondly, the renal veins may become so engorged with blood from the relief of both intra-abdominal and intra-ureteric pressure that the kidneys may stop work, with consequent anuria. A single catheterisation is often sufficient to enable the patient to pass water again naturally. If not, the procedure must be repeated every six hours until the bladder is empty, twenty ounces being drawn off each time, and after that be passed at least three times a day. F. K.

TREATMENT OF DISEASES OF THE DUCTLESS GLANDS

DISEASES OF THE THYREOID GLAND

Thyreoid Medication.—For the treatment of disease by means of thyreoid extract there are two golden rules: one, to keep the dosage, especially the initial dosage, as low as possible; the other, to maintain a close supervision of the patient. The method so much in vogue of giving 3–10 gr. three times daily cannot be too strongly condemned. The initial dose should never exceed $\frac{1}{10}$ – 1 gr. three times a day, and even so a careful watch should be kept for symptoms of intolerance. It should never be forgotten that the more urgently in need of thyreoid extract a patient stands the smaller will be his tolerance of it. Tachycardia, high temperature, mental symptoms, emaciation, vomiting and diarrhœa are all indicative of a high degree of intolerance, and their appearance carries with it a suggestion of grave mismanagement. The recumbent pulse-rate should never be allowed to go above ninety-five, and when the temperature rises to normal the drug should be suspended for a time. It is a safe plan, especially when giving thyreoid extract over long periods of time, to intermit the treatment for one week in every four. In the case of women, it is as well to arrange that this interval shall coincide with the menstrual period. The first subjective sign of thyreoid intolerance is a consciousness of the heart's action, unaccompanied, however, by anything approaching tachycardia. Another frequent sign is a coryza very similar to that provoked by iodide of potassium. In the case of children a reliable guide is provided by the weight chart: as long as weight rises the drug is well borne; when it becomes stationary the drug should be suspended; while a falling figure is invariably a sign of intolerance and calls for discontinuance of the treatment.

The effect of thyreoid extract is considerably enhanced if it is exhibited in combination with three other drugs, namely, iodine, arsenic and calcium. These may be given in a mixture—

℞ Calcii iodid. gr. v
Liq. Arsenicalis ♏ ii
Aq. Chlorof. ad. ℥ ss ter post cib.

which should be suspended every fourth week coincidently with the thyreoid extract.

It is always advisable to modify the diet of a patient under treatment with thyreoid. The amount of meat foods and of alcohol should be very much reduced and salt should be excluded from the dietary. In all forms of thyreoid inadequacy muscular asthenia is present, sometimes in a very high degree. For this reason massage is as beneficial and as grateful as general exercise is harmful and unwelcome.

Success with thyreoid therapy is dependent, and to an extent which is not always realised, upon the employment of a reliable preparation. The tabloids of Messrs. Burroughs and Wellcome are made in minimal doses of $\frac{1}{4}$ gr. (equal to 10 gr. of the dried extract) and they are entirely trustworthy. Elixir Colloid (Squire) is a liquid preparation of great reliability. Its form permits of minute dosage, while its name effectually conceals its identity from the laity —a point of no small importance when dealing with cases of a certain class.

Thyreoid Inadequacy.—Minor degrees of thyreoid insufficiency are of far commoner occurrence than is generally assumed to be the case. Babies who do not thrive are frequently the victims of such a condition; they can sometimes be made to improve by the judicious exhibition of a combination of thyreoid extract and grey powder. Rickets, adenoids, nocturnal enuresis, enlarged glands, a tendency to "catch" anything which is going about, all suggest a state of subthyreoidism in children. Such a state may be congenital, or it may be the outcome of the starvation of the gland by one of the febrile diseases incidental to childhood. True influenza is a severe thyreoid depressant and recovery is both easier and more rapid where thyreoid extract is exhibited during convalescence. States of minor thyreoid inadequacy are frequently seen in women at puberty, at menstruation, during pregnancy and lactation, and at the menopause. Thyreoid medication is invariably beneficial in these conditions. Pregnancy makes a very prolonged demand upon the resources of the thyreoid gland and, in consequence of the subsequent reaction, the mother is frequently unable to suckle the infant. Here again a careful thyreoid medication sometimes works wonders, not only in promoting the secretion of milk, but in materially relieving the difficulties incidental to the post-partum state. Certain forms of obesity (see article on *Obesity*), which make their appearance towards middle life in men as well as in women, yield to thyreoid extract given in small doses in combination with other measures. Many of the stigmata of old age point indisputably to an exhausted thyreoid gland; such are the chilliness, dry skin, baldness, slow pulse-rate. In cases where there is no reason to suspect the condition of the heart and the arteries, judicious, *very* judicious, thyreoid medication will sometimes produce a sense of well-being in these old people to which they have long been unaccustomed.

Nocturnal Enuresis.—Nocturnal incontinence of urine in children may be the outcome of a variety of predisposing causes of which by far the commonest is thyreoid inadequacy. In the vast majority of cases it will be found that children who habitually, or even frequently, wet their bed are undersized; that they have a high arched palate and imperfect teeth; and that they suffer from a subnormal temperature which is lowest at night. All these signs inevitably point to a lack of the internal secretion of the thyreoid. The condition is best treated by thyreoid extract or by the salts of calcium, whose property it is to stimulate thyreoid activity. In certain cases both methods may be combined with advantage. Thyreoid medication should be initiated with extreme caution. A half grain tabloid (Burroughs and Wellcome) once a day is a safe dose for a child of five, and, if well borne, may be gradually increased until the child is taking ½ gr. three times daily. A careful watch should be kept upon the pulse and temperature and upon the weight. A rise in all three is an indication that the dose is sufficient; a fall in weight shows that it is excessive. As long as the temperature remains subnormal thyreoid may be exhibited; as soon as the night temperature reaches the normal caution is necessary. The pulse-rate should never be allowed to exceed that proper to the age of the child, and the onset of a sudden and violent nasal catarrh should be taken as a warning to suspend treatment. Upon all counts it is wiser to suspend the treatment for one week in every four, and this applies equally to calcium, arsenic and iodine, whether exhibited alone or concurrently with the thyreoid extract. For reasons already given a mixture such as the following is a valuable reinforcement to thyreoid treatment, and in minor cases may alone suffice to control the enuresis. The dosage is estimated for a child of eight years.

℞ Calcii Iodid. gr. ii
Liq. Arsenicalis ♏ ii
Tr. Nucis Vom. ♏ ii
Syrup Aurantii ʒ i
Aquam ad. ℥ ss.
M. sig. ter die post cib.

Patience and perseverance are factors of cardinal importance in the management of nocturnal enuresis. Unless these little patients are encouraged to form regular habits the most perfectly calculated system of medication is liable to prove disappointing in its results. Incontinent children should not only empty the bladder before going to bed; they should be aroused once in the night between ten and twelve, and they should be made to micturate immediately upon waking in the morning. This warning is the more necessary as children who wet their bed are frequently lethargic and unenterprising. Moreover, nocturnal incontinence is apt to be regarded by both mother and nurse either as a visitation from the hand of God against which it is useless to strive, or as a transient phenomenon which the child will "grow out of."

In spite of the general success of a thyreoid therapy in nocturnal enuresis, there is a small proportion of cases which, though characterised by all the appearances of thyreoid inadequacy, do not respond to treatment. It is probable that some gland other than the thyreoid is here at fault. Suprarenal extract in doses of 20 to 30 drops a day has been employed with success for children of four to fourteen years of age. Pituitary has so far proved useless, though the results obtained with thymus seem to be encouraging. Belladonna or atropine should be employed only when all other means have failed.

Myxœdema and Cretinism.—Both myxœdema and cretinism are the expression of pronounced thyreoid insufficiency. Treatment consists in the nicely calculated exhibition of thyreoid extract. In the case of the cretin, the earlier it comes under treatment the better will be the results obtained. Under careful management the bodily development proceeds at a pace and to a degree which is very striking, while the improvement upon the mental side is little short of marvellous. Conditions closely resembling cretinism and myxœdema are occasionally provoked by some error in function on the part of the hypophysis. For this reason, in cases which prove intractable to thyreoid the treatment should be supplemented by the exhibition of hypophyseal extract. Where the treatment by thyreoid extract not only fails to ameliorate the condition but produces symptoms of intolerance, it should be discontinued and hypophyseal extract employed in its stead. The best method is the intramuscular injection of 1½ gr. of the fluid extract three times a day. It should be remembered that this has a marked effect in raising blood pressure, which, unless the patient is carefully watched, may rise to a figure which is dangerously high.

Infantilism.—Several types of infantilism are recognised, and all are referable to absence or insufficiency of function on the part of one or more of the internal secretory glands. The actual causative factors are not, however, as yet identified. Hence treatment resolves itself into a more or less tentative endeavour to re-establish the deranged balance by supplying or supplementing the supposed failing secretion. Thyreoid extract should always be given first, and if this fail recourse should be had to pancreatic extract, which has been warmly

recommended in this connection. Hypophyseal extract should also be tried, that is the extract of the anterior lobe, or an extract of the whole gland.

It is well to remember the beneficial influence of fresh air, good plain food, and light warm clothing in all conditions which in any way approach infantilism. Red meat and alcohol should be excluded from the diet, and physical exercise should always be well short of fatigue. On the other hand, massage two or three times a week is a valuable adjunct to treatment, and a warm bath at night (100° F.) induces sleep and promotes metabolism.

Inflammation and Enlargement of the Thyreoid Gland.—Under certain physiological conditions, such as puberty, menstruation and pregnancy, the thyreoid gland sometimes enlarges and becomes tender, as if in response to an increased demand. Such hypertrophy is frequently only transient and passes off as the condition to which it owes its origin subsides. On the other hand, the symptom may persist and may prove to be the commencement of a goitre. In the case of pregnant women the sign is significant. It constitutes a warning that the supply of thyreoid secretion is insufficient for both mother and child, and serious harm may result if this warning goes unheeded. Thyreoid extract should be exhibited in small doses and, unless the symptom disappears, the treatment should be continued during the entire term of pregnancy.

That the thyreoid becomes enlarged in all febrile conditions is well known. This is especially the case in typhoid fever, and the condition has been observed in malaria and in cholera. Congestion and inflammation of the thyreoid gland are by no means infrequent accompaniments of true rheumatism. Here the enlargement may become so severe as to give rise to pain in swallowing, dyspnœa and pressure effects of varying degrees of intensity, while the inflammatory process may even involve the trachea and the glottis. Mild degrees of inflammation are effectually treated by means of hot fomentations. Where the inflammation is severe and threatens to spread to the neighbouring structures, thus giving rise to dyspnœa and dysphagia, blood should be withdrawn by the local application of leeches. Three or even four should be used and these are best applied along the lower border of the inflamed area in such a way that the scars will later be concealed by the clothing. If these measures fail there is no alternative but to invoke the aid of the surgeon. Prompt surgical intervention is always indicated in one rather rare condition. I refer to those cases sometimes seen after typhoid fever, where the inflammatory process leads to suppuration.

Goitre.—If we exclude exophthalmic goitre and malignant disease, goitres may be of two types : (1) parenchymatous, and (2) adenomatous. Combinations of both forms are frequently encountered.

Goitre is endemic in certain districts. It is believed that infection is due to an amœba and that it is conveyed in the drinking water. Where the disease is slight and the patient young, he should at once be removed from the infected area. Failing this, it is indispensable that the water for his consumption shall be obtained from another and uncontaminated supply. The most valuable drugs are iodine and its preparations and thyreoid extract. Either method should be employed with extreme caution and the initial dosage should be kept low. Five min. tincture of iodine and 5 gr. potassium iodide given three times a day is sufficient to start with, and this dose may be gradually increased to three or four times the amount, provided always that the patient does not show signs of intolerance. In the case of thyreoid, 1–2 gr. in the course of the day is an ample initial dose, and this may be increased to 5 gr. a day if the pulse-rate does not become unduly high. In some cases better results are obtained if the iodide and the thyreoid are exhibited simultaneously. The local application of Ung. Potass. Iodid. may assist in reducing the size of the tumour, and a compress of adrenalin to the gland at night is a good adjuvant to treatment by the mouth. Mention should be made of McCarrison's vaccine treatment, which is said to produce very striking results.

Exophthalmic Goitre (*Graves's Disease*).—Under suitable treatment, the prognosis of Graves's disease may be said to be good as to life, but bad as to recovery. In a few isolated instances spontaneous recovery has been recorded, but such cases are rare. The tachycardia, which is so characteristic a feature of the disease, frequently leaves behind it an enlarged left ventricle and a blood pressure which remains persistently above the normal. Moreover, the mental associates of Graves's disease are of bad or very doubtful prognosis and, even where the physical symptoms have yielded to treatment, it is uncertain whether the patient is ever again to be trusted upon the mental side.

Treatment consists first and foremost in rest, both mental and physical. This point cannot be too strongly urged, especially as, in view of the restlessness and unreasonableness of patients suffering from Graves's disease, the conditions are difficult to obtain. The patient should be kept in bed for weeks or even months; even in very slight cases recovery will be far quicker if the patient will be persuaded to go to bed for a time. Once there she should be kept

there by hook or by crook, until the pulse-rate is normal or nearly so. A large, light room should be chosen with windows open day and night. Anything in the nature of physical exertion must be avoided, and the patient must be carefully shielded from worry and from mental excitement of all kinds. In view of the emaciation, sometimes considerable, by which Graves's disease is accompanied, the diet, though plain, should be generous. Little meat should be given, and alcohol should be rigorously excluded.

Typical Graves's disease is a condition of thyreoid excess and almost certainly of thyreoid perversion; as a general rule, therefore, thyreoid extract should not be exhibited. Pituitary and parathyreoid extracts have both been known to do good. The same may be said of bile salts, given by hypodermic injection. A valuable adjuvant to this treatment is a compress of a solution of adrenalin applied to the gland. The application of X-rays to the gland is warmly recommended by certain physicians of repute. The method is said not only to reduce the local enlargement, but materially to ameliorate the general symptoms of the disease. Inasmuch as the internal secretion of the thyreoid and that of the pancreas are in many respects antagonistic to one another, pancreatic extract in large doses ought theoretically to be helpful in Graves's disease. The results of such treatment have not, however, so far seemed encouraging. Belladonna and aspirin are sometimes useful in tiding over emergencies, but their continued employment is not to be encouraged.

Surgical intervention in Graves's disease is very rarely desirable. Mild cases will usually respond to medical treatment, and severe cases are not suitable for operation, as they most frequently succumb. It is the general experience that the mortality after operation for Graves's disease is extremely high. L. W.

DISEASES OF THE SUPRARENAL GLANDS

Addison's Disease.—This disease occurs only as the result of slow destruction of the suprarenal glands, that is of all parts of the gland, both cortex and medulla.

Animals survive experimental removal of the glands for one or two weeks. A few days after the operation weakness and loss of appetite appear, and together with that the phenomena of a lowered circulation with feeble, rapid heartbeat. The picture is clear and simple: there is nothing to suggest poisoning or aught else than depression of the circulation and loss of its driving power. Under such conditions any external strain may overpower the weak heart and suddenly determine death. On the other side may be quoted the extraordinary power of adrenalin, the active principle of the suprarenal medulla, to raise the blood pressure when injected within the veins. The deduction seems clear, that the muscular tone of the heart and blood-vessels depends on the suprarenals. Vasomotor nerves control the tone, this way and that: they do not alone maintain it, for animals readily survive removal of the visceral and vascular nerves. It is not the damage of the neighbouring nerves but the loss of the suprarenal glands in Addison's disease that leads to circulatory failure and death.

The consequent weakness of the heart governs every detail of the treatment of the patient. Unfortunately no drugs have been found to be of enduring value to raise the cardio-vascular tone. Digitalis and pituitary extract are alike of little avail, for the muscular tissues in the absence of the suprarenals react to therapeutic agents in an entirely abnormal way.

General Lines.—Physical rest must be as complete as possible, the heart being treated as carefully as it would be in the cardiac irregularities that may follow diphtheria. Lengthy examination of the patient should always be avoided. It has been proved that emotional anxiety or anæsthetisation rapidly exhaust the suprarenals of animals. Hence it is obvious that the small store of adrenalin in these patients must be husbanded by protecting them from all mental distress. Anæsthetics and surgical shock are highly dangerous.

Warmth is all important, and indeed is craved for by the sufferers. Provided that it does not cause a sense of chilliness, open air treatment may be employed.

Food must be frequent, light and nourishing. Alcohol in moderate quantities may give a satisfactory sense of *bien être*. Cod-liver oil and malt extract should be tried with caution, since they often excite nausea.

For the damaged gland itself nothing can be done. Addison's disease does not develop until both the glands are infected, so that it is impossible to contemplate surgical excision of either. Tuberculin is said to be harmful, perhaps by causing such a local reaction in the glands as to choke the scanty output of adrenalin by which life was just maintained.

Syphilitic disease of the glands has never been diagnosed and specifically treated. In cases of simple fibrotic atrophy the process may chance to stop, and the patient be spared for an invalid life.

But treatment cannot at present discriminate between these conditions. All that can be done is to husband the patient's strength by general and symptomatic measures, and hope that the pathological processes may abate—as does indeed occur in a few rare instances—before the glands are utterly destroyed, for death in that case must be the issue.

Organo-therapy, unfortunately, has not yet been found to be efficacious. On the rapidly advancing cases it certainly does not exert any definite benefit, just as no treatment succeeds in keeping glandless animals alive. Transplantation of gland tissue into the kidney or elsewhere may in time be found practicable and useful; but at present such surgery has shown nothing to justify the risk of the operation.

Nevertheless suprarenal extract is always worth a trial. The customary dosage is probably too small. If it is permissible to regard the aim as simply that of making good a deficiency of adrenalin, then it is necessary to know what is the daily output of adrenalin from normal glands. The glands of a healthy man contain together at least 10 mg. of adrenalin: the excretion of it into the blood stream is rapid and frequent, so that the amount consumed daily is probably large. A case of double thrombosis of the suprarenal veins, which the writer once observed, survived about two days. One might, then, conjecture that at least 3 mg., that is, 3 c.c. of a 1000 solution, should be supplied daily.

There may be advantage in using an extract of the entire gland. The dried gland is apt to lose its potency, and it is better to use fresh extract. A fresh sheep's gland—kept on ice until required—is ground up with saline solution and glycerine, filtered through muslin after standing half an hour, and the filtrate, which is fairly palatable with the sweet glycerine, at once taken. A rough rule is that 1 gm. of the entire gland contains 2 mg. of adrenalin, so that one or two glands may be taken daily. The commercial forms of adrenalin, whether extracted from the glands or the synthetic lævo-suprarenin, may also be given in 1 mg. (15–20 min. of 1 in 1000) doses t.d.s. well diluted with water after food. If it causes vomiting the treatment should at once be stopped.

For subcutaneous or intravenous injection only the pure principle should be employed. Adrenalin borate, in 0·5 or 1 mg. doses, rather than the chloride should be chosen for hypodermic administration, because the latter salt causes pain at the site of injection. The result is a rise of temperature and of blood pressure for the first day or two but, in the writer's experience, no lasting benefit. Intravenous injections, 1 mg. in 500 c.c. of normal saline, might be of value in critical periods, when the oft-quoted danger of inducing atheroma is negligible. It must not be forgotten that adrenalin is a poison, causing fatty changes in the kidney and liver, or death by coma when given in large quantities.

Symptomatic.—The general weakness and sense of coldness are met by general measures. Loss of appetite requires nux vomica, or occasionally arsenic. Pain in the epigastrium is rarely more than an uneasiness, but every endeavour must be made to save the patient even this discomfort. Constipation is to be controlled by petroleum emulsion, mild salines, or purgative pills. Strong cathartics or enemata may induce fatal collapse. Diarrhœa demands bismuth, opium and hot applications to the abdomen and buttocks.

Vomiting is among the worst of symptoms and the most difficult to treat. Bismuth, dilute hydrocyanic acid, drop doses of tincture of iodine, or champagne may be successful. Gastric lavage is to be deprecated, if it distresses the patient. Arguing that the vomiting might be due to over-action of the vagus in the failure of the sympathetic inhibitor nerves of the intestine, the writer in one case tried full doses of atropine, but without avail.

Acute syncopal attacks require hot applications over the precordium, strong coffee and brandy internally, and especially the intravenous injection of adrenalin. In animals the restorative effects of adrenalin on the heart are astonishing, though not enduring.

Suppression of urine occurs whenever the blood pressure falls to 60 mm. or so; but it calls for no special notice or treatment.

Other Diseases.—Brief mention may be made of some other pathological conditions that affect the suprarenal glands, though none of them call for special treatment. There is no evidence at present to justify the acceptance of a special group of clinical features as indicative of exaggerated suprarenal secretion, and there is certainly no hypertrophy of its medulla in cases of high blood pressure.

Hæmorrhages destroying the glands are not rare, for example in meningitis, infectious fevers, etc. They do not appear as a rule in purpuric conditions, and they are much more frequent in the fragile tissues of childhood. Surgical manipulations in the region of the kidney are at times done with a heavy hand, and the writer has seen a suprarenal completely destroyed by the resulting hæmorrhage in its lacerated substance. A man can, however, live perfectly well with a single suprarenal.

Simple adenomata of the cortical cells are often seen as yellow, fatty nodules embedded in the medulla. They develop at middle age, and occur especially in cases of interstitial nephritis or of tuberculosis. In the latter disease at autopsy they are sometimes mistaken for areas of tuberculous infection. They are innocent, insomuch as they do not cause pressure atrophy of the true secreting gland cells.

Malignant growths originating in the supra-

renal in adult life are not recognised until their characteristically hæmorrhagic secondary deposits occur in lung or in bone, and they have no special clinical picture apart from these deposits. But those occurring in young children being either sarcomatous or truly derived from the cortical gland cells, are in the latter case liable to be associated with remarkable precocity of sexual growth. Excision of the primary mass has always failed to save life on account of the early dissemination of secondary nodules.

T. R. E.

DISEASES OF THE HYPOPHYSIS CEREBRI

1. ACROMEGALY

In considering the treatment of acromegaly it is well to remember that the progress of the disease varies in its course and effects in different cases. It may be more or less rapid, or it may extend to thirty or forty years or more. Much will depend upon the occupation, position in life and habits of the patient. Its symptoms are many and varied; some being due to the effect of the alteration in size and function of the hypophysis cerebri, many are consequent upon the derangement of organs and regions arising from the thickening growth and pressure of their bony surroundings.

Many of the subjective phenomena, as well as nutritive and structural changes in soft tissues, arise indirectly from those causes. It may be that some of the circulatory changes are due to the influence of reflex effects of pressure upon nerves in their course. Integrity of the hypophysis cerebri seems essential for the control of the trophic nerves.

The headache, neuralgia and giddiness associated with the disease may be due to defects of vision that progressively arise and the congested and inflamed state of the membrane lining the ethmoidal and frontal sinuses and the nose, all due to, or aggravated by, the expansion, growth and distortion of the bones in the neighbourhood of the hypophysis cerebri consequent upon its growth and functional alteration. Much relief is afforded by careful correction of the vision from time to time by glasses. The ophthalmic surgeon is often the first to diagnose a case of acromegaly, as his help is sought early for the astigmatism so frequently present. This has to be corrected with suitable cylinders, but changes are periodically required owing to the alterations which may come on in the axis while the eye-ball is being squeezed or pressed upon by the thickened conchal bones,

Suitable applications by spray or douche to the nasal cavities and their neighbourhood will remove their secretion and discharges, and tend to reduce the hyperæmia and inflammation of them, which is associated with the hypertrophied bones and sinuses.

The douching of the nasal cavities is especially beneficial before going to bed, as it often enables the patient to have a good night which he might not otherwise have.

The treatment of the hypertrophied erectile tissue with the galvano-cautery will lead to its contraction and increase of the nasal airway. Sometimes when the airway is much obstructed by the more or less hypertrophied conchal bones, some bone may be advantageously removed.

Demulcent lozenges relieve the dryness of the tongue, which may amount to soreness, consequent on the mouth-breathing which is unavoidable when the nasal airway is much obstructed. Liquorice combined with menthol and eucalyptus is most useful and comforting. Menthol lozenges are so soothing in their effect also upon the headache and faceache that they appear to have a direct action upon the hypophysis cerebri. They may be used as a substitute for tobacco, for which the acromegalic generally has an intolerance.

The many drugs that have been used with varying success for the headache, neuralgia and "queer feelings" complained of in the course of the disease, include aspirin, phenacetin, phenalgin, quinine and morphia. The danger of giving morphia in such a chronic disease is obvious. It is to be avoided. Aspirin seems to be the most reliable notwithstanding that in some people it may increase the lethargy and depression which must be considered.

The greatest relief is derived from absolute rest—immobility—or allowing the tendency to sleep, which is a characteristic of the disease, to assert itself.

Several acromegalics have told the writer that "drugs may help, but I know I can get relief if I sit still for twenty or thirty minutes with my eyes closed."

The headaches are lessened in frequency and extent by care in diet, great moderation in exercise and the avoidance of much movement or shaking of the head, or conditions, such as vibration, from any cause, that may give rise to similar effects.

For the trophic changes in the feet a most useful treatment is the daily use of an electric footbath during the cold weather, as has been recommended by Dr. Lewis Jones, the bath consisting of a tub of warm water with an electrode of copper-plate at each end, and the battery of a simple me al induction-coil of smooth action, regulated to be as strong as can be borne with comfort. If used for a week or two now and then, it will improve the circulation in the feet and prevent, or even cure, the trophic ulcers liable to occur during the winter,

when the lower extremities so frequently suffer from local asphyxia or syncope.

The skin of the toes should be hardened by frequently painting them with friars' balsam.

The faradic footbath, besides having a local effect, is decidedly a tonic. More than anything else it improves the circulation and braces up the mucous membranes. It will influence the nasal catarrh and even cut short the severe colds in the head to which the acromegalic is so liable, besides having its effect on the lethargy and the fearful feeling of fatigue and weakness so characteristic of the disease.

The alterations in the mouth, produced by the growth of the lower jaw, and the want of apposition between the upper and lower teeth, will require the dentist's attention, which may also be of use in causing an early diagnosis of the disease. This is all the more necessary as the teeth are liable to be ruthlessly extracted owing to their malposition. Suitable metal dentures should be worn, capping the upper molars and filling up the gap between them and the lower ones. A fresh " bite " will thus be provided and the patient's digestion will benefit. The denture must be modified periodically as the jaw grows and advances. The patient's teeth will thus be saved, an advantage later on, as under the influence of the disease they are known to become extra hard and strong.

For the hypertrophied heart with the irregular pulse the line of treatment indicated is that of ordinary heart disease. An occasional course of digitalis or strophanthus (2 or 3 min. of the tincture) three times a day for a week or two, will steady the heart, improve the pulse and add to the patient's comfort. Small doses should be given, and for a short time only. This is important as the acromegalics are not very tolerant of drugs or alkaloids of any kind, including tea, coffee and tobacco.

The use of the faradic footbath already mentioned has a decidedly beneficial effect on the heart. The enlarged heart and the weakened muscles call for great moderation in exercise, and avoidance of fatigue.

Many are the drugs which have been used and good results have been obtained from putting the patient through a course of arsenic, quinine, iodide of potassium and even mercury. Of late, attention has principally been given to the glandular extracts, including the thyreoid, the testicular and the hypophyseal extract, but it is difficult to judge how far any improvement is actually due to the drug, owing to the uneven course which the disease runs, with great diminution and, at times, subsidence of some of the subjective symptoms. Dr. G. H. Gibson, of Edinburgh, has found the hypophyseal substance beneficial in some early cases and in later stages has found it relieve a number of subjective symptoms.

Thyreoid extract given in 5 gr. doses twice a day for several weeks has made the patient feel more comfortable and had a decidedly tonic effect. It is more reliable than hypophyseal extract, which, however, may raise the patient's blood pressure. The two extracts have been given in combination with apparently good results. Hypophyseal extract is certainly contra-indicated in certain stages of the disease when there is a state of hyperpituitarism and in some cases has been distinctly harmful. It has generally been given in tabloids of 2 gr. two or three times a day.

Operative Treatment.—To the difficulty of reaching the hypophysis cerebri, so deeply situated, and removing the portions of it which are diseased, or any new growth in the fossa hypophyseos, has to be added the danger of the wound becoming infected when it is made through unhealthy tissues, since the air passages are invariably unhealthy in acromegaly. The question is also increased by the difficulty of saying at what period of the disease it is justifiable, and the needlessness of operating in a case which runs a benign course, and in which later on most of the troublesome symptoms may subside. It seems only justifiable in a case which develops rapidly with acute symptoms, and in which the intense headache, the amaurosis, the vomiting, all point to a quickly growing tumour, possibly a sarcoma, at the base of the brain. The removal of it may save the patient's life. In some cases relief of the headaches has followed a trephining operation. Dr. Harvey Cushing has found that a subtemporal decompression is indicated to meet the general pressure disturbances. He has lately suggested in cases of profound secretory insufficiency the transplantation of a gland from another source. L. M.

2. OTHER DISEASES OF THE HYPOPHYSIS CEREBRI

The thyreoid gland presents problems for treatment in connection with: (1) excessive secretion and overgrowth, that is, exophthalmic goitre; (2) adenomata and colloid cysts of relatively inactive gland tissue, which are liable to hæmorrhagic distension and so produce symptoms connected with mechanical pressure on adjacent structures; (3) atrophy and secretory failure, with consequent myxœdema.

Very similar are the diseases of the hypophysis cerebri. Parallel to exophthalmic goitre is *acromegaly*, and just as the former disease may years later be succeeded by symptoms of myxœdema, so too is acromegaly liable to drift ultimately into a condition of hypopituitarism.

Adenomatous growths cause only pressure symptoms. Arising from the substance of the pituitary, they grow within the narrow confines of the fossa hypophyseos beneath the tightly stretched diaphragm of the dura mater. Symptoms of bitemporal headache arise from the tension of the dura; of loss of part of the visual field, especially a temporal hemianopia, from the pressure of the growth on the optic chiasma; and of actual hypopituitarism because the non-secreting adenoma compresses the true secreting cells. When the diagnosis has been established, the treatment is surgical. Headaches may be controlled by phenacetin and such drugs; but pressure on the optic nerve requires early relief. As the loss of vision is caused by direct pressure on the nerves and is not associated with optic neuritis, recovery after a successful operation may be good.

The method of approach elaborated by the American surgeons, Halstead and Cushing, causes no disfigurement of the face. The upper lip is everted, and an incision an inch long made into the mucous membrane across the labial frenum. From this a submucous tunnel is driven up the septum nasi, by removal of the vomer, and through the sphenoid bone to the base of the fossa hypophyseos. The dura covering the gland can then be opened by a cruciform incision. This mere release from pressure, a sellar decompression, suffices to allay the bitemporal headache, and may even restore vision, since it enables the growth to take a path of less resistance downwards into the naso-pharynx. The pressure may, however, be so great as to necessitate removal of part of the mass.

Larger tumours may burst through the diaphragma sellæ and, growing rapidly, give the general phenomena of cerebral tumour as well as blindness: these cases, with optic neuritis and signs of frontal or temporal lobe involvement, require a large cranial decompression. After decompression by either route, X-rays should be used to check the progress of the tumour.

Hypopituitarism is suggested when, in addition to showing the localising features of a glandular tumour, the patient becomes obese, lethargic and asexual. For this glandular therapy is required, either with or without a surgical decompression. Transplantation has not been proved to be of value. The gland extract may be taken by the mouth or injected subcutaneously. By the mouth, tablets containing 3 gr. of the entire dried gland of an ox or the equivalent of 6 gr. of the fresh moist gland may be taken t.d.s. The dose is raised until the patient exhibits slight glycosuria when given a test meal of 150 gm. glucose. No harmful results have been reported even with such huge quantities as 100 gr. t.d.s. of the dried glands.

Thyreoid extract may be used in addition. (See also *Diabetes Insipidus*.) There is no justification for trying adrenalin. T. R. E.

INFANTILISM AND SENILISM

For the purposes of treatment **Infantilism** may be divided into two great classes, in the one of which the cause is known and in the other is unknown.

Among the causes of infantilism the toxins undoubtedly hold a very important place, and in the word toxins we not only include the poisons of the infectious fevers, of tuberculosis, of syphilis, of malaria, but also the extrinsically formed toxins such as lead and alcohol. Evidently, therefore, each of these must as far as possible be eliminated before we can successfully treat any particular case of infantilism. Toxins exert a stunting effect upon development in one of two ways. They may act as starvation acts by giving rise to general debility, or they may exert a local effect upon some organ which ordinarily stimulates or controls development. The debilitating effect of the toxins may to some extent be counteracted by the more liberal administration of food during the course of a fever. Thus from this point of view it is important that no starvation tactics should be adopted in the treatment of acute rheumatism, of enteric fever, or indeed of any other microbial disease during infancy and childhood. It need hardly be added that the ordinary sanitary measures of a sufficient food supply, of fresh air, of cleanliness and of congenial surroundings are of capital importance in the treatment of all cases of infantilism.

Increasing attention is being directed to the significance of certain organs as centres for the regulation of growth and development. Chief among these are the thyreoid, pituitary, hypophysis cerebri, suprarenal, thymus and sex glands. In the symptoms which gather about any particular case of infantilism it is usual to find some which are predominant and are at the same time indicative of disturbance of one of these glands above all others. It is to these dominating symptoms that our efforts at treatment should be directed. Thus, if with a sluggish intelligence there is general lethargy with fatness, sensitiveness to cold, and a physiognomy suggestive of cretinism or myxœdema, extract of the thyreoid gland should be given, beginning, it may be, with one grain doses once a day and gradually increasing as in any ordinary case of cretinism or myxœdema. If fatness be the most conspicuous symptom it may be suspected that the hypophysis is inactive and that the infantilism is the expression of an

adiposo-genital dystrophy. In such cases Cushing advises that the whole hypophyseal gland should be given, beginning apparently with as many as fifteen fresh ox glands a day, or with their equivalent in the dried extract. It has been estimated that this remedy if given subcutaneously is four times more effective than if given by the mouth. In another case pigmentation of the skin, asthenia and a low blood pressure may point to the suprarenal glands as the chief defaulters, in which case adrenalin should be given. This is best administered subcutaneously. Overaction of the thymus gland is shown most decisively by the appearance of symptoms of lymphatism, and should at once be met by the administration of small and gradually increasing doses of thyreoid extract, by the application of the X-rays to the manubrium sterni, by reduction of carbohydrates and by an increase in proteins. Sometimes backward development of the sex organs is the most conspicuous feature, and in these cases marked improvement often results from the giving of thyreoid extract, even in cases in which there is no reason to suppose that the thyreoid gland is the first or chief offender. Infantilism is sometimes associated with signs of pancreatic incompetence, and is markedly improved by the use of the pancreatic extracts. Herter has described a similar form of infantilism in which he believes the defect of development resulted from the absorption of toxins from a too-flourishing intestinal flora. He has in these cases obtained good but variable results by careful dieting and by general hygienic supervision.

Generally speaking any case of infantilism is capable of improvement so long as ossification of the long bones is incomplete. It is, therefore, advisable that an X-ray examination of the state of the epiphyses should be made before beginning treatment, and that another examination should be made if the progress is not satisfactory.

Infantilism which has no perceptible cause (Ateleiosis) has hitherto met with no effective treatment. Nevertheless thyreoid extract should invariably be tried in those cases in which the symptoms are suggestive of thyreoid inadequacy and hypophyseal extract in those with obesity. Possibly the use of the latter remedy in larger doses than have hitherto been given may prove more effective. Apparently it is not possible to give an overdose of hypophysis by the mouth.

Senilism.—Morbid prematurity of the declining stages of development, like infantilism, may be the result of syphilis, of alcohol or of any severe or persistent intoxication. It may also be due to prolonged hardship, to excessive toil or worry, or indeed to any of the causes of premature old age if inordinately prolonged or carried to an extreme degree. Evidently, therefore, the prevention or treatment of senilism is identical with the prevention or treatment of old age. One need only add that no reliance whatever must be placed upon sour milk or upon any bactericidal or operative treatment directed to any part of the intestinal tract, and that temperance is as conducive to old age as the liberal use of food is conducive to vigorous youth and maturity.

Of that sensational and bizarre form of senilism which comes on without apparent cause and is termed Progeria, little can be said in regard to treatment, for nothing has hitherto seemed to be of any avail in arresting the inevitable progress of the disease from its onset in babyhood to its termination in premature senile decrepitude in youth.

H. G.

TREATMENT OF DISEASES OF THE BONES AND JOINTS

OSTEOMALACIA, ACHONDROPLASIA, HYPERTROPHIC PULMONARY OSTEO-ARTHROPATHY AND OSTEITIS DEFORMANS

It must be insisted on that all these are merely names for but little understood conditions in which the bones of adults become soft and yielding so that they very readily bend or break. We are familiar with the museum appearances of the bones, and we know other facts about them—for example: (1) That in the extreme condition known as osteomalacia, where the lower part of the skeleton and more especially the pelvis becomes like putty, pregnancy is the rule; (2) that achondroplasia is most certainly a disease which arrests the growth of the epiphyseal cartilages once they have become active; (3) that osteo-arthropathy is associated with wasting pulmonary disease, frequently tubercle; (4) that osteitis deformans is frequently associated with new growths of the bone and is attended with overgrowth of bone in some parts, associated with weakness in others.

Besides these facts we must not lose sight of a medley of other allied conditions, as, for example—

Von Recklinghausen's Disease, a fibrous degeneration of a bone—or bones—of unknown causation although readily diagnosed by skiagraphs.

Neurotrophic atrophy of bone observed in

anterior poliomyelitis, tabes, syringomyelia, epilepsy.

Fragilitas Ossium—a mere name to a symptom; including probably widely different conditions.

For all these strange and bizarre alterations in the adult or growing skeleton there must be a cause, and until that cause is recognised and placed on a sure foundation treatment is entirely empirical.

In general terms we may speak of terminating the pregnancy in osteomalacia—a confession of complete ignorance, of rest, fresh air, calcium salts, cod-liver oil, organic phosphorus compounds, etc.

I would, however, suggest that in some way all these diseases have a common origin, that is, some defective metabolism or retrogressive changes or atrophy in the anterior lobe of the hypophysis cerebri (pituitary gland); such a suggestion is by no means devoid of evidence to support it. We recognise that growth of much of the body as well as the metabolism is controlled by a complex arrangement in which the nervous system takes a share and which largely depends, in some cases, on various forms of internal secretion, as, for example, of the sex glands. What more natural than to believe that such an important part of the body as the skeletal structures own some similar control.

It is well recognised that the anterior and posterior lobes of the hypophysis cerebri are widely different in origin and in functions, and that "the anterior lobe is related to the general growth of the body, and especially of the skeleton, whilst the posterior lobe, which includes the pars intermedia, probably serves to promote the contractility and increase the tone of plain muscular tissue generally, as well as of the heart, and to excite the activity of certain glands, viz. the kidney and mammary glands" (Schäfer).

Experimental evidence also is not entirely wanting, for—

1. Ascoli and Legnani, in their records of experimental hypophysectomies, mention the occurrence, not only of undergrowths of bone, but of spontaneous fractures.

2. H. G. Turney, *Neurology* (March 12, 1913), reports a case of spontaneous fracture of the sternum associated with pituitary degeneration; a similar case has been reported by Langdon Brown.

3. Erdheim and Stumm describe enlargement of the hypophysis cerebri in pregnancy, chiefly due to the presence of finely granular cells in the anterior lobe of the gland, widely differing from the natural cells, and *in some cases almost taking their place completely.*

Clinical evidence is sparse.

A case of osteomalacia has been reported where a perfect cure was effected by the administration of hypophyseal extract.

The author of the present article has given fresh anterior lobe or preparations of the mixed gland (chiefly posterior lobe) in five cases with marked success in every case. Two of these were clear cases of Von Recklinghausen's disease, with failure of union of fractures—in both cases despite repeated surgical interference. In both cases, on the administration of hypophyseal extract the fractures united and there was no further trouble. A like satisfactory result was obtained in three cases of so-called "fragilitas ossium." These cases will be published later.

With regard to treatment, it must be remembered that these are only tentative suggestions. To the writer's knowledge no observations have been made post mortem on the state of the anterior lobe of the hypophysis in such cases—and skiagraphy in the few cases here noted has given no definite result; such rare cases may, however, provide an infinitely rich field for research, and it may well be that much more common skeletal defects may owe their origin to the same source.

It would appear that there is little danger of overdosage. The whole anterior lobe of a fresh *lamb's* hypophysis has been given three or even four times in the week.

The anterior lobe may be obtained in a dry condition from both Messrs. Burroughs Wellcome and Parke Davis, but the very great expense of the preparation is a serious bar to its continuous use.

Now that the posterior lobe is in such frequent use it should not be difficult to obtain the anterior lobe at a reasonable cost.

Hypertrophy of the Gland.—Here, the converse of the above. The hormone which controls and stimulates the growth and nutrition of the bones is held to be produced in excess. The suggestion has been made that this produces gigantism and acromegaly, and that the difference between the two is that in gigantism the hypertrophy of the gland has commenced before the activity of the epiphyseal cartilages has come to an end, while in acromegaly the hypertrophy of the gland has commenced after the ankylosis of these cartilages. J. K. M.

CHRONIC INFECTIVE DISEASES OF THE JOINTS

Recent researches into the etiology and pathology of chronic joint affections have led to the differentiation of various types and so paved the way for their more rational therapy.

Tuberculous and gonococcal types of arthritis do not fall within our survey and will be considered elsewhere.

We shall include (1) gouty, atrophic and hypertrophic arthritis, rheumatic, infective, and villous varieties; (2) neurotrophic and hæmophiliac joint lesions, also intermittent hydrarthrosis and syphilitic joint diseases.

The confused nomenclature existing renders a reference to the salient anatomical features of these disorders desirable.

By *Chronic Rheumatic Arthritis* or articular fibrositis is understood an inflammatory exudate into the peri-articular tissues with resultant fibrous hyperplasia, either localised or diffuse, but unattended by changes in the articular surfaces.

Villous Arthritis is marked by chronic inflammatory changes leading to numerical increase and hypertrophy of the synovial tufts. It is scarcely a definite clinical entity, but common to many forms of arthritis. Still cases occur, usually resulting from direct or indirect trauma or strain which show no other joint disease.

The term *Infective Arthritis* is here applied to chronic non-purulent types—unassociated with any specific germs—the morbid changes being due to toxins derived from a remote infective focus.

Usually they consist in a periarthritis without articular or bony changes, and differ from atrophic arthritis in their predilection for the larger joints, and the paucity and erratic distribution of the articular lesions.

The treatment of chronic joint disease involves two principles : (1) correction or amelioration of the underlying pathological condition—some warp of metabolism or some autotoxic or infective process; (2) local therapy of the actual joint lesions.

Treatment of Group I

A glance at the many different clinical varieties contained in the first group shows that the articular lesions are but local manifestations of some general disorder, which calls for treatment. Almost all these forms of chronic arthritis are held to be toxic or infective in origin, so that our first duty is to institute a careful search for any source of toxic absorption.

Localised Foci of Toxic Absorption. — Oral sepsis, pyorrhœa alveolaris, or some suppurative process in the tonsil, middle ear or nose, may be the infective focus keeping the joint mischief active. A thorough examination of the mouth and naso-pharynx is imperative. If sepsis exists stumps should be extracted, cavities cleansed and filled, tartar removed, and unhealthy gums attended to.

During inspection artificial dentures should be removed, so that concealed stumps be not overlooked. The use of antiseptic washes, peroxide of hydrogen, etc., reinforced by thorough brushing and "silking" of teeth should be insisted on. Recurring attacks of tonsillitis with exacerbations of joint trouble should suggest the propriety of excision. The nasal passages are more rarely a source of absorption, but when responsible we have seen the happiest results follow their expert treatment.

Nor should we forget to examine the rectum for signs of ulceration, to exclude this source of toxic arthritis. The genito-urinary tract in both sexes should be exhaustively investigated. The urine and fæces should be bacteriologically examined, as recent researches have shown that inoculation with autogenous vaccines of predominant organisms, when present, has sometimes proved most beneficial. Lastly, we should look for any signs of tubercle, as some forms of rheumatoid arthritis are possibly of aberrant or attenuated tuberculous nature.

Dietetic Treatment

It is in chronic polyarthritis of diathetic or autotoxic origin that dietetic modifications are chiefly called for.

Gouty Arthritis.—In many instances all that is needed is mere reduction in the quantity of nourishment taken. In subjects prone to excess we should prescribe plain fare calculated to dull rather than to whet appetite. In such persons a purin-free diet, apart from its intrinsic merits, is desirable because of its unappetising nature. In the matter of quality the most common digestive disability relates to starchy and saccharine foodstuffs, when bread, potatoes, milk, puddings, should be restricted or temporarily withdrawn. In the absence of special indications a mixed diet of meat, fish, game, poultry, with moderation in starchy or sweet foods, will prove the most suitable.

As a rule gouty persons should affect simple fare, avoid second helpings or many courses, and take very little condiments and salt. Alcohol many gouty persons find it easier to abstain from than to be abstemious, and for such abstinence should be advised. In strict moderation alcohol in my experience does not appear more harmful to gouty than to other persons, but while not advocating its use, I do not hesitate to order it in atonic types, giving preference to well-matured spirits or light sound wine. For flushing purposes two or three pints of water daily should be enjoined; if the water is hard, distilled aerated water, or some slightly mineralised natural water, is preferable.

Atrophic Arthritis. Syn. *Rheumatoid Arthritis.*—In the absence of gastro-intestinal derangements good nourishing food up to the limits of digestive capacity is indicated. Thorough mastication, regular meal-times, a

restricted intake of fluids during their progress, with rest before and after repast should be enjoined.

During progressive phases comparative intestinal asepsis should be aimed at by prescribing some days fasting in bed with nothing but hot water, or a little milk diluted with lime, soda or barley-water, and as a change, junket, cream, soured or butter milk.

When improvement sets in a lacto-farinaceous regimen may be instituted, and continued pending the control or disappearance of any intestinal putrefaction present, when a gradual return to a mixed diet may be permitted. More frequently, however, there is enfeebled capacity for digesting carbohydrates. A temporary reduction or withdrawal of these foodstuffs is then necessary, the patient partaking freely of red meat with abundance of hot water until the tendency to acid fermentation is overcome, when a mixed diet may be resumed.

These primary indications having been fulfilled, we may next consider the dietary best calculated to counteract the remote consequences of acid fermentation.

For, as in rickets, the acid products of fermentation are neutralised at the expense of calcium, ammonium, and other elements in the tissues. Moreover, as I pointed out some years ago, the symptom complex of hyperthyreoidism is frequently associated with rheumatoid arthritis. Now excessive thyreoid secretion is frequently correlated with a lowered tolerance for glucose which favours excessive calcium excretion.

This calcium leakage should be made good by abundance of lime-containing substances. Fats are highly desirable, such as fresh butter, cream, dripping, bone marrow, fat bacon and suet puddings, olive oil or cod-liver oil either plain or in the form of an emulsion or with malt preparations, but care should be taken not to disturb the digestion by an excess. Moderate quantities of fresh green vegetables should be eaten regularly, with strict moderation in farinaceous foods.

Sir James Barr emphasises the importance of acid fermentation with consequent decalcification in rheumatoid arthritis. He prohibits oatmeal, all acids, acid fruits, rhubarb, tomatoes and asparagus, and prefers glucose and honey to cane-sugar or jam. He considers saccharin preferable to sugar if the urine has become alkaline under treatment. Of fruits he favours grapes, bananas, nuts, prunes and figs, and discountenances sweet and acid drinks, also wine and malt liquors.

Except in progressive phases I have, however, found that malt liquors agree well, and as a substitute Horlick's Malted Milk is very useful; in all cases I encourage the free ingestion of milk.

While as a rule a diet rich in calcium is indicated, Hirschberg has shown that in some instances there is deficient urinary excretion of calcium. To determine this he places his patients on a diet containing 1·8 gm. of calcium derived almost entirely from milk. If, after resting in bed for three days only 10 per cent. or less of the ingested calcium is excreted, a calcium-free diet is indicated. For this he gives white and aleuronate bread, sago, rice, cornflour, oatmeal, tomatoes, mushrooms, meat soups and extracts, beef, fowl, calves' liver, tongue, etc.

He also gives foods rich in sugar, honey and jams, vegetable butter substitutes, distilled water, white beer, port wine, champagne. He cautions against rash withdrawal of calcium, save after a metabolic test, but considers that a trial is justifiable even when this is not feasible. Under careful control of urinary excretion and body weight he continues the diet from six to eight weeks, but even at the end of this period milk, butter, yolk of eggs, potatoes, and spinach are rigidly excluded. Extended observations, however, are necessary to decide between these opposing views.

To sum up, our primary dietetic indications in rheumatoid arthritis are to diminish or arrest any tendency to intestinal fermentation or putrefaction, and subsequently to raise the resistance of the individual by as nutritious and varied a diet as can be assimilated.

Hypertrophic Arthritis. Syn. *Osteo-arthritis.*—In the widely generalised cases sometimes met with in young persons, an abundant and nutritious diet is indicated.

In middle-aged subjects dietetic modifications are frequently called for, as gout is sometimes superimposed.

In obese subjects with osteo-arthritis of the lower limbs a reduction cure to lessen strain on the diseased articulations is advisable. Carbohydrate and fatty foodstuffs must be limited or temporarily withdrawn. Bread should be toasted, milk and butter abstained from, and sugar replaced by saccharin.

Meat, fish, game, poultry and vegetables save the roots and tubers are permissible. Clear soups are allowable and salads devoid of beetroot or oil. Alcohol is undesirable, but if taken a good sound whisky or light dry wine is most suitable.

The intake of fluids during meals should be forbidden or strictly limited and reserved to the end of the meal. Hot water should be taken one hour before or two hours after meals for flushing out.

Lastly, osteo-arthritis is frequently associated with arterial atheroma, so that the benefits of a decalcified dietary should not be overlooked.

Chronic Rheumatic, Infective and Villous Arthritis.—It is impossible to prescribe a diet suitable for all such cases.

The subjects of articular fibrositis are frequently gouty, 28 per cent. of a series analysed by A. Bassett Jones and myself showing definite stigmata of this. In such treatment along those lines will prove the most satisfactory. Others lacking such frank avowals of their gouty tendency nevertheless pass urine of excessive acidity, containing a high percentage of uric acid. Their food habits should be scrutinised, for no improvement takes place until the acidity of the urine is diminished.

Purin antecedents, especially beef, beefsteaks, and sweetbreads, should be greatly reduced or withdrawn, and a regimen consisting largely of milk, vegetables, cheese, butter, nuts and white bread substituted. Such a diet is also suitable when there are evidences of intestinal putrefaction.

If obese, a diet similar to that advised for reduction of body weight in osteo-arthritis is indicated and is especially beneficial when the joints of the lower extremities are affected.

In villous and infective types we should also control or arrest any tendency to intestinal putrefaction or fermentation, or to obesity.

General Treatment.

Climate.—The ideal for arthritic patients is one characterised by low relative humidity, a small rainfall, and abundance of sunshine.

Damp surroundings and sudden variations in temperature aggravate their pains, but dryness, warmth, and equability are invariably beneficial.

In winter, if possible, resort should be had to Upper Egypt, Algiers or the French Riviera. Failing this, an inland bracing climate with residence on gravel or sandy strata, and little subsoil water is advisable.

Clothing.—Flannel underwear is undesirable, being non-absorbent. Woollen garments of not too heavy texture afford protection against sudden fluctuations in temperature, and are suitable to those who lead a strenuous outdoor life. For others less exposed, woven linen or silk undergarments may be recommended. More important than the nature of the clothing, especially in so-called "rheumatism," is the necessity of changing the underwear whenever damp from perspiration, neglect of this being a fertile source of relapses.

Rest and Exercise.—In exacerbations of all forms of chronic arthritis, rest must be attained by complete or partial fixation of the affected joint. Otherwise regular exercise, short of fatigue or strain, is beneficial, special caution being observed in regard to osteo-arthritis and villous arthritis. Erratic or excessive exercise is inadvisable and readily precipitates acute attacks. In rheumatoid arthritis systematic exercises should be insisted on. Where the shoulders are involved the use of weights and pulleys is desirable, and for stiffness and rigidity of the fingers, knitting, wood-carving, piano-playing, etc., should be regularly undertaken. Movements entailing supination and pronation of the forearm are especially called for. Where the knees and ankles are involved, exercise may be obtained through the medium of a bicycle fixed on an appropriate stand. Lastly, whenever possible, the treatment available at a well-managed Zander Institute should be obtained.

Massage and Passive Movements.—These form an essential part of the treatment of chronic arthritis. In polyarthritis of gouty, rheumatic or autotoxic origin *general* massage is of the greatest value. Under its influence the circulation improves, waste products are more freely excreted, the nerve centres gain tone, and marked improvement in health ensues.

The actual joint lesions, if subacute, should not be subjected to direct massage, this being particularly true of osteo-arthritic, rheumatic, and villous types. Deep massage of the limb above the joint is of the greatest value, its derivative action causing diminution of the œdema, hastening absorption of fluid, while muscular spasm is lessened.

In chronic gouty and rheumatoid arthritis *direct* as well as *derivative* massage is most beneficial, especially after previous exposure to hot-air, vapour or electric baths, which relax the tissues and diminish their sensibility.

Carefully regulated passive movements and resistance exercise should be simultaneously employed, these being of inestimable value in chronic joint affections.

Hydrotherapy, etc.

All chronic joint diseases are eligible for hydrotherapy at some period, but its administration requires care and discrimination, as much depends upon the personal equation, the state of the nervous and circulatory functions being the chief controlling factors.

Thus, gouty arthritics are often of an irritable neurasthenic type, and therefore intolerant of extremes of temperature, and in such hypothermal or sedative applications are most suitable. But the subjects of chronic rheumatism or rheumatoid arthritis often suffer from torpid circulation with sluggish vascular response, and here stimulant measures, either by heat or cold, or in sequence or alternation are indicated.

The corpulent arthritics react more feebly than the spare, yet bear prolonged hydrotherapy much better. Thin persons react well, but often become exhausted and suffer from

secondary chill and other untoward consequences.

We should try and train these patients to react favourably to the more stimulating effects of cold or hypothermal applications, the value of which in chronic arthritis is greatly underestimated.

For cold baths stimulate oxidation processes, and in many forms of chronic arthritis there is deficient oxidation of protein, and of fat also. Although caution is necessary, it is quite possible in most cases by carefully graduated baths or douches to obtain the good effects of cold as well as of thermal applications.

General Hydrotherapy.—Whole body exposure is indicated in polyarthritis due to some warp of metabolism or some toxic state of which the joint lesions are but local manifestations. Acute phases or exacerbations are unsuitable for hydrotherapy which should be restricted to the subacute and chronic stages.

Subacute Stage.—Hypothermal baths (92°–97° F. for 15–30 minutes) are indicated, with douches of low pressure to sensitive or painful joints. In gouty arthritis with high arterial pressure a course of baths at 93° F. combined with fan douches after the Bourbon-Lancy technique often proves beneficial.

Such neutral baths are of great value in vasomotor instability, *i. e.* in rheumatoid arthritis with evidences of hyperthyreoidism—quickened pulse, tremor, etc., and in gouty arthritis occurring in women at the menopause. Their sedative action is of signal service in chronic arthritics suffering from insomnia or irritable skin affections. Of natural mineral waters those of Buxton, Ragatz, and Baden-Weiler fulfil the requirements.

Chronic Stage.—Here stimulant and resolvent methods are needed to effect absorption of exudates, reduce swelling, and increase mobility. Thermal waters are most effectual, and *ceteris paribus*, the higher the temperature the greater their excitant action. Of natural thermal waters those of Bath, Aix-les-Bains, Gastein, and Wiesbaden are in great repute. Simple immersion baths (98°–106° F.) with or without massive undercurrent douches (110°–115° F.) should be employed.

Soolbader or natural thermal or cold *brine* waters exert a similar excitant effect, and are obtained at Droitwich, Builth, Harrogate, Strathpeffer, and Llandrindod.

Aix and Vichy Massage.—These procedures profoundly influence metabolism and hasten the elimination of toxic and waste products. Combining the influence of massage and warm temperature, they are extensively used in gouty and rheumatic arthritis, and in arthritis deformans.

Terminal treatment by cold is essential to counteract their enervating after-effects and to secure a tonic result.

I usually employ a circular needle douche, reducing the minimal temperature each time until a temperature of 90°–70° F. is reached. This is especially necessary in rheumatoid arthritis, where the good effects of Aix massage are increased when followed by the tonic action of cool or cold applications.

But in many instances of this affection the abdominal musculature is very flabby with a tendency to visceroptosis and low blood pressure. Here a Vichy bath is preferable to Aix massage, the former raising while the latter tends to lower arterial pressure.

This also determines our selection of Aix or Vichy massage in gouty arthritis, but any tendency to phlebitis negatives them, immersion baths being better. In articular fibrositis direct massage and douching are highly beneficial, unless there be a tendency to villous formation; also in osteo-arthritis the joints are better left alone, and the rubbing restricted to the surrounding muscles.

Vapour Baths are contra-indicated in the old and feeble, and in the subjects of advanced cardiac or renal disease. Being powerfully eliminative they are of special value in chronic toxæmic cases, viz. articular fibrositis, gouty arthritis, and osteo-arthritis, especially in the obese. In chronic arthritics with harsh, thickened or irritable skin vapour baths are preferable to applications of hot air or radiant heat. For eliminative effects a bath at 120° F. for fifteen to thirty minutes is necessary, but as a means of heating the skin prior to an Aix or Vichy bath, or some cold application, an exposure of three to five minutes at 120° F. is sufficient. At Bath, Aix-les-Bains, Luchon, and elsewhere, natural vapour baths are in great vogue, their local effects being enhanced by immediate massage of the affected joints.

Local Hydrotherapy. Dry Douches.—These are chiefly useful in localised arthritis, whether gouty, rheumatic, traumatic, infective or villous.

Relief of Pain.—Extremes of temperature and pressure being inadvisable, we should begin with a tepid fan douche 80°–92° F. at a low (4–8 lb.) pressure, replaced later by a hot 104°–110° F. rain or spray douche of 10–15 lb. If the pain is obstinate a combination of hot and cold douches is often effectual. The hot stream is first directed on to the joint at a temperature as high as can be comfortably borne. Impinging only on a small area a temperature of 110°–120° F. can be gradually reached, and according to individual tolerance maintained for two to four minutes, when the skin becomes dusky or purplish red. At this point a cold douche 70°–60° F. or lower is played on to the joint for five to thirty seconds.

This is turned off directly the dusky red hue gives place to a scarlet tint, which occurs as passive distension of blood-vessels is replaced by active dilatation.

Our object being to obtain a derivative or sedative rather than a tonic or stimulant effect, the cold douche should stop short of producing pallor and chilliness of the skin, as, in that case, the subsequent reaction would certainly aggravate the pain. A broken jet, fan or spray douche, 3–15 lb. pressure, should be used, strong percussion effects being undesirable.

To relieve Stiffness and Swelling.—Where pain is absent and active mischief has ceased, stimulating applications are indicated. Alternating jets or sprays are most suitable, the hot and cold douches being each from fifteen to thirty seconds' duration. The more remote the extremes of temperature and the more abrupt the transition from hot to cold, the greater the excitant effect.

Dry Massage Douche.—Simultaneous massage greatly reinforces the stimulating and absorbent action of douches. If the skin be sensitive a neutral douche is indicated; but otherwise very hot (115° F. and upwards) or very cold (65° F.) ones may be used at a high pressure.

Very hot or very cold douches are contra-indicated if the joints are inflamed, congested or extremely painful to pressure. In the absence of such indications a cold percussion douche of high pressure (20–30 lb.) is of exceptional value in long-standing cases with exudation, rigidity and limitation of movement. Coincidently the related muscles should be massaged.

Hypothermal or cold douches are very valuable in degenerative arthritis with atony and relaxation of ligaments. Where there is great sensitiveness to cold, a hot rain douche or a local hot air or electric light bath will render the patient more tolerant of a subsequent cold application.

Fortunately, hot douches (104°–120° F.) at high pressure are like colder applications, stimulant in their action, and may be employed when hypothermal douches are inapplicable.

Wet Douches.—In this procedure the patient is immersed in a bath 98° F. or higher while an undercurrent douche 110°–115° F. is played on to the painful joint—a cushion of water intervening so as to moderate the impact. The same principles as for dry douches apply, but it is chiefly valued for its analgesic effects.

Peat, Mud and Fango Baths.—Out of these substances partially solid baths of varying density are produced which are capable of general or local application. Apart from the varying degree of hyperæmia produced by their thermic action, mud baths probably owe their efficacy to their radio-active qualities. Uranium mud or actiniferous earth, a by-product of uranium ores, has been used in the treatment of chronic joint affections. Compresses and pads of the mud, or baths containing 8 oz. to 40 gall. of warm water have been employed, the pads being applied for several hours.

General peat baths range in temperature from 98°–112° F. with a duration of twenty to forty-five minutes, and when the higher temperatures are used a subsequent cold application is indicated. At Postyen, Acqui and Battaglia whole body baths of fango are given at a temperature of 104° F., but for local applications 120°–122° F. may be used. Local peat and fango baths relieve pain, promote absorption, and increase mobility. With strict attention to detail valuable results in localised chronic arthritis may be achieved.

Treatment by Hyperæmia.—Active hyperæmia by superheating is more suitable for *chronic* forms of arthritis than passive.

We may use non-luminous or luminous hot-air baths; of the former either Tallerman-Sheffield, Greville or Tyrnauer systems; of the latter the incandescent light bath or the Dowsing modification. All admit of *general* or *local* application.

General.—Exposure of the whole body is preferable in polyarthritis of diathetic or toxæmic origin.

In cabinets *heated by steam or gas* a temperature of 180° F. usually induces profuse sweating. Exposure for twenty to thirty minutes is ample, and elimination is aided by free ingestion of water during the bath, and subsequent envelopment in blankets.

In Greville baths, as in the foregoing, the temperature should be gradually raised to perspiration point, usually from 250° F. upwards, and then maintained at this level for twenty to thirty minutes, then slowly lowered, the process occupying one hour.

Greater heat (350°–400° F.) can be endured, but scorching ensues unless the parts are adequately protected by asbestos lint or towels.

Besides sweating a fall in arterial pressure occurs, with increased output of urea and uric acid.

I am convinced that for whole body exposure Tyrnauer baths possess no advantage over Greville baths.

Hot air exposures should be followed by a sponge or immersion bath or tepid spray lowered from 98° to 80° or 75° F. They are valuable in gouty or rheumatic arthritis, especially if complicated by obesity, but are contra-indicated in arthritics with skin eruptions, advanced nephritis, cardiac weakness, and in rheumatoid arthritis associated with Graves's disease.

Radiant Heat or Light Baths.—For general exposure these are superior to hot-air baths, as the luminous rays penetrate the deeper

tissues, especially the combined incandescent and arc systems. A greater reaction also occurs at a lower temperature, perspiration appearing in three to five minutes often at a point below normal body heat. Also luminous baths raise body temperature higher than non-luminous and stimulate the oxidation of protein more, while perspiration is induced more quickly at lower temperatures and more profusely than in vapour, Russian or Turkish baths. Extreme heat is unnecessary, 110°–130° F. often sufficing, though higher temperatures can be employed in selected cases.

Light baths are especially valuable in polyarthritis of rheumatic or gouty nature, and in osteo-arthritis if complicated by gout or obesity. In chronic arthritis accompanied by psoriasis or other skin lesions they are superior to non-luminous baths.

They are of great service in rheumatoid patients to prepare the skin for the tonic effects of hypothermal or cold applications. For this purpose short exposures to stimulate the skin but not to evoke sweating suffice, and they should be followed by a graduated cold spray or circular douche. In these after-applications excessively low or abrupt changes are to be avoided, or aggravation of pain ensues. In hyperæsthetic subjects I have found the substitution of blue for white incandescent lamps more soothing.

Where feasible I always prefer a light to a non-luminous bath for whole exposure, and after a prolonged bath for eliminative purposes prescribe an immersion bath 90°–85° F. for three minutes, or a tepid douche of same duration. But in robust subjects, a bath from 70°–60° F. or a short sharp douche 60°–55° F. may be given for a few seconds.

Local Hyperæmia.—This is more suitable when the joint lesions are few and local. *Non-luminous* baths seem more efficient in absorbing exudates because of the more intense hyperæmia produced.

Within reasonable limits the higher the temperature, the greater the hyperæmia, but extremes are unnecessary.

The tolerance of patients is not always a safe guide owing to diminished sensibility of the skin, hence caution is necessary in arthritics with arterio-sclerosis and diabetes in gouty subjects. The temperature should be gradually raised short of producing pain. With a Tyrnauer bath in from six to eight minutes 170°–200° F. is reached, and according to the case it should be maintained at this level twenty to thirty minutes, then gradually cooled, the process lasting forty-five to sixty minutes. This fulfils all requisites.

Local Light Baths are perhaps more useful in degenerative types of arthritis. Temperatures above 200° F. are rarely required, and their duration should be from half an hour upwards.

In villous arthritis of the knees so commonly associated with varicose veins, I have been impressed by the improvement not only in the joint but in the accompanying infiltration by a course of light baths.

After-treatment is important if the best results are to be attained. The effects may be prolonged if the joint on removal is wrapped in cotton-wool and covered with rubber cloth and flannel; this is useful in very chronic arthritis, and both bath and compress may be used twice daily. Where stiffness rather than pain is present the parts should be massaged and passively exercised while still perspiring. Hot-air or light baths are an excellent prelude to ionisation in gouty or villous arthritis and articular fibrositis. Where the shoulder is affected I have found a leucodescent light most convenient for applying the preliminary radiant heat. When more stimulating effects are desired cold friction with the wet hand or towel, a brine rub, or a prolonged cold douche may be applied.

Electrotherapy.— Both hydro-electric and Schnee four-cell baths may be used, the former for general, the latter for local application.

The baths are given at from 97°–100° F. and should not exceed twenty minutes' duration. The strength of current should be carefully regulated, and sudden or erratic changes guarded against.

Drugs can be added to the water in the cell of the Schnee bath, hence it is very useful where treatment by ionisation is desirable.

Ionisation.—The simplicity, relative painlessness and certainty with which the " ions " can be directed to the diseased part make this method a great advance over the older liniments and ointments whose action for the most part is superficial. (For technique see article on *Electrotherapeutics*.)

For *analgesic* effects a 2 per cent. of sodium salicylate should be used, with pads of ample size closely adapted to the joint and attached to the negative pole.

Stronger currents are necessary with salicylic ions, varying from 30–40 ma. to 150 or 200 ma., which may be used in the case of the knee. Such strong applications according to Lewis Jones are inadvisable more than twice weekly, lest injury to the skin ensue.

The foregoing method is useful not only in painful joints, but also in the referred pains such as the crural neuralgia, which often accompanies osteo-arthritis of the hip.

Ionisation with lithium and iodine, the former salt on the positive and the latter on the negative pole is beneficial in gout, rheumatoid arthritis and articular fibrositis; œdema and

swelling diminishing while the mobility is increased.

Repeated applications are essential of twenty to thirty minutes' duration, the current being gradually raised to 40–70 ma. The efficacy of ionic medication is greatly increased by a preceding exposure to radiant heat.

In *Post-Inflammatory Ankyloses* such as follow infective arthritis, chlorine ions introduced at the negative pole influence nutrition, and help to resolve cicatricial tissues, which, at the same time, part with the sodium ions.

A 1–2 per cent. solution of sodium chloride is used, with a current of 100 ma. and over, two or three applications being made weekly. According to Leduc if the case prove obstinate the sclerolytic action of iodine should also be enlisted in alternation with chlorine ionisation.

Ionic medication in all its forms is more effective in superficial joints such as those of the hand, wrist, and knee, than in the hip and shoulder, and in all chronic joint affections large currents and long séances are usually necessary to obtain the best effects.

High-Frequency Currents.—The efficacy of the thermal action of electricity as produced by high frequency and *diathermy*, like that of "static wave currents" is due to hyperæmia. If the diathermy apparatus be employed, the heating effects obtained are still more marked owing to the larger currents available.

These methods are often combined with radiant heat or ionisation, and it seems probable that diathermy will prove an agent of extreme value in the various forms of chronic arthritis.

Apart from local application *general* electrisation by high-frequency and statical machines has been enlisted to correct the defective nutrition underlying many forms of chronic joint disease.

Lastly, we may allude to the fact that recently local exposure of the joints to X-rays in rheumatoid arthritis has been advocated by Chisholm Williams for alleviating pain and swelling.

Medicinal Treatment.

"Gouty Arthritis" (*see Article on Gout*).

"Rheumatoid" Arthritis.—This condition is now assumed to be the outcome of a chronic toxæmia of gastro-intestinal origin.

The principles of treatment therefore involve (1) the reduction or prevention of toxin formation, (2) the diminution of the degree of toxic absorption.

To control the production of toxins alterations in diet or judicious fasting with copious hot water drinking are the most effectual measures, and as adjuncts, though not as substitutes, for such dietetic modifications we can enlist the aid of antiseptic substances.

During *febrile* phases the sulphate or hydrochloride of quinine (5–10 gr.) should be given with dilute hydrochloric acid—a deficiency or even total absence of free HCl being often demonstrable during exacerbations.

In marked gastric irritability salicylate of quinine 1–5 gr., with salicylate of bismuth 5–20 gr., sometimes succeeds better.

Where the evidence points to intestinal fermentation or putrefaction β-naphthol or its salicylate 5–10 gr. should be given in a cachet with salicylate of quinine or bismuth, or suspended in an almond oil mixture.

In *apyrexial or quiescent* stages the same principles should guide us—correction of abnormal fermentative or putrefactive processes and speedy elimination of their toxic products.

So far studies at the Royal Mineral Water Hospital have revealed neither absence nor deficiency of free HCl in non-progressive cases. Still clinically, in common with others, I have found dilute hydrochloric and nitro-hydrochloric acid in combination with nux vomica of great utility, probably because dilute acids tend to stimulate the formation of secretin and so augment pancreatic secretion.

If the urine is but slightly acid or alkaline with pathological deposition of lime salts as a result, a mixture of dilute phosphoric acid with acid phosphate of soda should be taken well diluted before the principal meals.

These patients often suffer from amylaceous dyspepsia with acid fermentation. In addition to carbonates of magnesia and calcium before food diastase 1–5 gr. or takadiastase $2\frac{1}{2}$ gr. may be taken in milk during or directly after meals in tablet or cachet form.

In such cases Sir James Barr advocates the bicarbonates of sodium and potassium with aromatic chalk 15–30 gr., in milk half an hour before meals, and a double dose at bedtime.

In hepatic sluggishness with intestinal putrefaction occasional courses of minute doses of calomel $\frac{1}{10}$ to $\frac{1}{8}$ gr. every two hours until 1 gr. is reached is very effectual.

For routine administration over prolonged periods Luff highly lauds a mixture of guaiacol carbonate and iodide of potassium, but my experience of it has not been encouraging.

All the foregoing measures aim at sterilisation of the intestinal tract, but they are futile unless supplemented by regular and thorough evacuation of the bowels. Chronic constipation is almost invariably present and a daily action is imperative, which if possible should be procured by mild laxatives such as confection of senna or sulphur, liquid paraffin or phenolphthalein. Where atony of the colon with stasis is present aloin $\frac{1}{4}$–1 gr., ext. nux vomica $\frac{1}{3}$ gr., ext. belladonna $\frac{1}{8}-\frac{1}{3}$ gr. should be given directly before the last meal. This may be

alternated from time to time with morning draughts of sulphate or phosphate of soda or other saline aperient. To secure more thorough cleansing of the colon high enemata of ichthyol and other medicinal substances may be employed.

At Bath and other thermal spas colonic irrigation by Plombières douches of radio-active water are in extensive vogue, but prolonged courses are necessary.

We would urge more thorough X-ray study of the intestinal tract in the constipation of rheumatoid arthritis, for more often than is at present realised there are displacements of the colon with delay in transmission of its contents.

The knowledge gained by skiagraphy as to the exact site of the stasis will enable us to supplement or replace purgation by intelligently applied massage. In the same way in visceroptosis, exercises and Swedish gymnastics and in some cases abdominal supports will do much to restore regular habits of evacuation.

Organotherapy.—Enlargement of the thyreoid, cold extremities, and Raynaud-like phenomena are common features of gastro-intestinal toxæmia, and some years ago I drew attention to their frequency in rheumatoid arthritis. For reasons detailed elsewhere I was led to administer thyreoid extract in such cases, with striking amelioration of the symptoms, an experience subsequently confirmed by many observers.

Daily doses of $\frac{1}{2}$ gr. are ample to begin with, and symptoms of hyperthyreoidism are to be guarded against.

Nathan has obtained good results with thymus gland in doses of 10–20 gr. three times daily over several months.

I have observed in some cases of rheumatoid arthritis symptoms suggestive of a polyglandular affection, and I note that Starkey advocates the intramuscular injection of an extract of pituitary, ovarian, and testicular extracts.

Relief of Pain.—Aspirin 5–10 gr. may be given three times a day, or if sleeplessness be a feature it may be combined with bromide of sodium 15 gr. Luff speaks well of aspirin in combination with pyramidon. In severe cases aspirin, phenacetin and Dover's powder, $2\frac{1}{2}$ gr. of each may yield better results.

Lastly, when all special indications have been met and nothing remains but debility, occasional doses of arsenic, nux vomica, syrup of the iodide of iron, or the compound syrup of the glycero-phosphates are the most reliable routine tonics.

Osteo-arthritis.—Treatment by drugs is purely palliative, and directed to the relief of special symptoms.

The drugs are much the same as those in chronic gouty arthritis, *i. e.* guaiacum, sulphur, arsenic, and the iodides to which may be added aspirin.

For the relief of muscular pain and stiffness so prominent in most cases I have found nothing that will mitigate it so certainly as guaiacum resin, tincture or powder in combination with sulphur. For marked swelling and intra-articular effusion iodide of sodium or potassium may be added with advantage.

When there are lesions in the lower extremities, obesity results from diminished capacity for exercise, and, as post-mortem examinations have shown, not infrequently uratic deposits are superimposed on the osteo-arthritic lesions. It is in these cases that the alterative and laxative action of iodide of potassium and guaiacum achieve so much benefit, this often being enhanced by the exhibition of small doses of colchicum. In middle-aged women, the subjects of osteo-arthritis of the knees, I have found the administration of thyreoid gland beneficial. The facies of many of these patients is strongly reminiscent of myxœdema, and I tentatively employed the drug upon an assumption of thyreoid inadequacy, always beginning with minimal doses. While the results in some cases were very striking, I was uncertain whether they were due to loss of weight or to some specific action on the local lesions.

In patients of pallid aspect and dry skin, arsenious acid or arseniate of soda $\frac{1}{60}-\frac{1}{30}$ gr. thrice daily is especially valuable for neuralgic symptoms, such as the sciatic or crural pain which often complicates osteo-arthritis of the hip. But for the immediate relief of pain, acetyl salicylate is perhaps the most reliable drug we possess. In broken-down subjects with widely generalised lesions nothing is superior to the syrup of the iodide of iron with arsenic and cod-liver oil or the compound syrup of the glycero-phosphates. "Chronic diseases need chronic remedies," and if any good or lasting results are to be obtained, drugs must be given perseveringly and over long periods.

Chronic Articular Fibrositis.—The causes are manifold. Some present definite stigmata of gout, or symptoms suggestive of such a tendency, *i. e.* heartburn, acid eructation, with strongly acid urine depositing urates. After a preliminary mercurial pill and saline purge a course of alkalies and diuretics is indicated.

We may use citrate of potassium or lithium to reduce the acidity of the urine, as usually the condition is not improved until this has taken place. When, as often happens, these subjects have torpid livers and are constipated, a pill containing 1 gr. each of the extracts of colchicum, aloes and rhubarb, with 2 gr. of extract of hyoscyamus may be taken at bedtime twice a week or even more frequently with

benefit. The addition of colchicum is specially indicated where the joints are the seat of pain and effusion. Free evacuation of the bowels is of paramount importance, and morning draughts of Condal, Apenta or Arabella water may be necessary. Diluents—weak tea, barley water, plain water or that of Evian or Vittel should be taken freely for their flushing effects.

If seen early enough this alkalising treatment often suffices, but if obstinate the addition of potassium iodide is indicated. The thin sallow type of patient is very sensitive to atmospheric variations, and apart from joint pains suffers from muscular and neuralgic manifestations. During exacerbations, diaphoretics—salicylate of sodium, aspirin, salicin, etc., with or without Dover's powder—often succeed admirably, if the bowels at the same time are freely opened by saline aperients.

With the decline of feverishness if the case proves obstinate guaiacum should be resorted to, this drug being especially useful in cases attributable to cold or damp. Where a stimulant effect is desired the ammoniated tincture with or without Infus. Cinchonæ or Decoct. Sarsæ Co. has in my experience proved very serviceable in the poorer classes.

If muscular or neuralgic pains are marked, Ammon. Chloridi 15–20 gr., Aspirin 5–10 gr., or Tinct. Cimicifugæ 20–30 min. in 1 oz. of Guaiacum mixture may be ordered thrice daily.

In obstinate cases that old-world remedy "Chelsea Pensioner," or tablets of guaiacum and sulphur, sometimes prove effectual when all other remedies fail.

In young, anæmic persons or the old and feeble the syrup of iodide of iron with arsenic and cod-liver oil will be found serviceable. The best results from drugs are obtained in the early stages, but where extensive fibrous hyperplasia has resulted they must be supplemented by intelligent and prolonged massage of the affected areas.

Fibrolysin.—It is convenient here to allude to the use of fibrolysin as a means of effecting scar tissue absorption in chronic arthritis with adhesions. This compound of thiosinamine and sodium salicylate may be injected intramuscularly (in the gluteal or deltoid regions) or hypodermically. It is not essential that it be injected over the affected area. Ampullæ containing 40 min. should be injected every two or three days, and thirty or more injections are usually required. An unpleasant degree of reaction often occurs, and the treatment is valueless unless reinforced by massage and passive movement or sodium chloride cataphoresis.

A similar therapeutic action is claimed for a combination of thiosinamine and antipyrine with eucaine lactate, which is said, moreover, to be non-toxic and non-irritating. A preparation of thiosinamine and iodine of unirritating character (iodolysin) is now available, not only for injection but also for oral use. Ointments and pigments of this same substance are also being used for external application in chronic arthritis, but whether absorption of fibrous tissue can be effected by this method is undecided.

Vaccine Therapy.—The association of oral sepsis and other infective foci with rheumatoid arthritis and other chronic joint diseases has led to the treatment of cases by autogenous vaccines.

In oral sepsis a strepto-bacillus has been isolated and vaccines prepared from it have improved and even cured rheumatoid and other forms of arthritis.

Goadby advises an initial dose of 10 millions, rising to 150 and 200 millions, given at first every ten days, then every fortnight for six months, and subsequently at intervals of six weeks for a year.

Carmalt Jones records good results with vaccines from streptococci obtained from the mouth in oral sepsis, and in others from the urine or fæces.

Crowe describes several "staphyloidcocci" (staphyloid because of their similitude to staphylococci), one of which, "staphyloidcoccus A," occurs with significant frequency in the urine of rheumatoid patients.

In cases of mixed infection by Bacillus coli or streptococci the subjects were first treated by vaccines from these assumed secondary organisms and subsequently one of coccus A was administered.

French physicians believe rheumatoid arthritis to be of attenuated tuberculous nature and report great benefit from the specific use of tuberculin.

As no causal relationship has been proved to exist between any one of these organisms and the morbid process, one may without prejudice remark that the vaccine therapy of rheumatoid arthritis as at present employed is of a rather haphazard description.

This probably accounts for the conflicting results obtained, and failure occurs in many instances.

In others relapses have been noted after great benefit and even apparent cure, an indication that the duration of the immunity conferred is limited. The prolonged course of the disease with its alternation of progressive and quiescent phases seems to point to its being due to an erratic series of auto-inoculations. It would, therefore, seem desirable to supplement vaccine therapy by controlling auto-inoculation by as complete muscular rest as possible.

While in this experimental stage vaccine

therapy must be tentative, and the initial doses small, it cannot be held to displace older and more reliable methods of treatment, though doubtless an adjuvant of great and increasing value.

External Medicaments.—These are used to relieve pain and stiffness and to promote absorption of inflammatory products. To increase the local circulation we may use poultices, fomentations followed by dry packs, heating compresses, hot-water bottles, or flannel bags containing heated salt, anodyne lotions, liniments or ointments. In more chronic stages alternate hot and cold compresses, or salt packs are useful for their stimulating effects.

In *gouty arthritis* attended by pain, alkaline opiate lotions are most efficacious, the saturated lint being covered with cotton-wool and oiled silk.

To promote absorption painting the joint with iodine or gentle inunction with iodine, vasogen or iodide of potassium with soap liniment are valuable.

In *rheumatoid arthritis* during exacerbations cold compresses may relieve more than hot fomentations. Other soothing applications are the liniment and compound ointment of methyl salicylate applied on lint covered with gutta-percha and flannel bandage. If the odour be objected to I have found a combination of amyl salicylate, menthol, and lanoline, or "Capsoline" as effective.

For peri-articular thickening non-staining iodine preparations such as "Iodex" are effective, also oleate of mercury 10 per cent., containing $\frac{1}{2}$ gr. of hydrochloride of morphine to the drachm. Blistering with "Canthos" plaster or light applications of the galvano-cautery are most valuable.

Prolonged counter-irritation of the spine in the neighbourhood of the cervical and lumbar enlargements with intermediate dressing of the raw surfaces with savin ointment as advocated by Latham and Middelton sometimes proves very beneficial in arresting progress of the disease.

In *articular fibrositis* for the relief of pain, poultices or fomentations are invaluable, and their effect may be increased by previously anointing the joint with compound methyl salicylate ointment, or it may be painted with tincture of iodine.

Or we may apply an ointment containing equal parts of salicylic acid, oil of turpentine and lanoline, afterwards covering it with gutta-percha tissue and flannel bandage.

Of other anodyne preparations amyl colloid, in my experience, is most useful, as when its soothing effects pass off the contained alkaloids may be stimulated to renewed activity by applying moist spongiopiline.

Or a mixture of chloral hydrate and camphor, with or without menthol, may be gently rubbed in or simply painted on and covered with oiled silk and a bandage.

For the absorption of thickenings oleate of mercury or one of the iodine preparations may be chosen.

The same principles should guide us in using these measures in osteo-arthritic, villous and infective arthritis.

Orthopædic and Surgical Treatment

Measures of this nature are chiefly demanded in villous arthritis, infective arthritis and arthritis deformans.

Villous Arthritis. — The knee joints are the site of predilection, and undue strain on these articulations is the commonest cause of this affection.

Weak, everted or flat feet are the static factors usually responsible. A pronounced sunken arch is easily recognised, but the slighter forms are more often than not overlooked, and both the knee and causal flatfoot diagnosed as rheumatism or gout.

Direct examination of the naked feet is essential to avoid error. In the absence of obvious sinking, pain on passive inversion, or adduction of the foot, with tenderness under the heel or navicular bone, usually indicates ligamentary strain. In slight cases suitable exercises involving inversion of the foot, with resistance movements to strengthen the anterior tibial muscles will probably suffice.

If such fail, or fixed distortion be present, it must be corrected mechanically by properly fitting boots with "skewed" heels or an efficient footplate.

Rectification of the static foot deformity is imperative. In severe cases wrenching of the foot under an anæsthetic and its retention by plaster in the fully inverted position until the parts are adjusted should not be shirked if other measures fail.

Obesity, if present, requires treatment, because of the static disturbances it produces.

Local treatment—hyperæmia, massage, ionisation, etc., is quite subsidiary to correction of the static fault. Firm bandaging or a snugly fitting knee-cap are more effectual in relieving pain. If such measures prove insufficient and the enlarged fringes give rise to symptoms of "locking" removal is indicated.

Even when complicating rheumatoid or osteo-arthritis, arthrotomy for the excision of villi has been attended with encouraging success.

Infective Arthritis.—The necessity for fixation in the acute stages leads but too often to the formation of adhesions.

Active hyperæmia, hydrotherapy and massage with early passive movements are, there-

fore, imperative. If excessive effusion is present, fixation of the joint and massage are indicated. If persistent, aspiration followed by closely applied webbing bandages may succeed.

At the same time the joints should be massaged, at first without movements, and with passive movements when the amount of fluid lessens. Any adhesions should be gradually broken down with or without an anæsthetic. Within twelve or twenty-four hours of this passive and active movements are imperative, and I have found the Zander system very useful in these troublesome cases.

Where muscular spasm with pain is a prominent feature, weight extension will probably relieve both symptoms, after any adhesions present have been broken down.

Atrophic Arthritis.—Until recently all surgical efforts in this domain dealt only with the sequelæ and not with the underlying cause of rheumatoid arthritis.

The growing conviction, however, that the disease is the outcome of intestinal stasis with resultant toxic absorption has culminated in a resort to surgical measures to combat its malign effects. Arbuthnot Lane emphasises the predominance of the motor defect, but, having regard to the tolerance shown by many persons for mere mechanical stasis, we cannot help feeling that an additional factor—chronic infection of the tract—also plays a part.

Needless to say, the heroic measures he advocates should not be entertained until all other means to correct stasis have been exhausted.

The anus and rectum must be carefully examined for any cause of organic obstruction. The exact site of intestinal block should be located if possible by X-ray examination. Upon the nature of the findings will depend our choice of procedure—appendicostomy with colon irrigation, short-circuiting operations or colectomy.

The results obtained by one or other of these measures have certainly been remarkable and would seem to point the way for their more extended employment in selected cases. But to our mind the true moral they point to, is, that we should be more alive to the evil potentialities of chronic constipation, more thorough and rational in our treatment of it.

In my work on Arthritis Deformans I have pointed out that the symptoms of intestinal toxæmia are invariably present *before* rheumatoid arthritis develops. In this prodromal period they constantly suffer from Raynaud-like phenomena, muscular cramps, sensory disturbances, pigmentation, and not uncommonly thyreoid enlargement. If during this initial stage our studies of the gastro-intestinal tract were more thorough and exhaustive we might reasonably hope to reach that ideal treatment of rheumatoid arthritis, its prevention.

Static Deformities.—Treatment as in Villous Arthritis.

Excessive effusion, if accompanied by pain, is relieved by aspiration with subsequent strapping.

Flexion of Knees.—If *slight*, great comfort may be derived by the use of a suitable cage admitting of flexion, but in which by means of an adjustable slot, extension is limited to a point short of causing pain. With the decline of acute symptoms the range of movement may be gradually increased. In *acute* flexion gradual rectification may be tried. Fat embolism, detachment of the patellar tendon, rupture of the popliteal artery with gangrene, have followed sudden forcible rectification. Modern experience favours open division or lengthening of the hamstrings with subsequent wearing of a retentive apparatus.

Arthrectomy of the knee and jaw has been practised with varying success for malposition and obstinate pain. Increased mobility of the elbow joints has been obtained by bilateral resection of the head of the radius.

Bony ankylosis of the knees has been overcome by double cuneiform osteotomy with open tenotomy of the hamstrings. Flexion and adduction of the hip joints has been corrected by bilateral subtrochanteric osteotomy.

The effects of persistent deformity and impaired motion are so pernicious that the question of operation, though still in the experimental stage, is worthy of careful consideration in selected cases.

Hypertrophic Arthritis. — Mechanical factors loom large in the genesis of osteo-arthritis either as causal or aggravating conditions. Therefore, any static deformity—flat feet, congenital, or acquired inequality in length of legs, etc.—should, if possible, be corrected.

For the actual joint lesions, fixation, absolute or partial, is necessary to prevent progressive bony proliferation with increasing mechanical limitation of mobility. If the joints are irritable, painful or swollen, complete rest is indicated, pending subsidence.

Knees.—According to the severity of the case firm strapping or bandaging, a well-fitting knee-cap, or retentive apparatus may be necessary. Aspiration for hydrops articuli is seldom called for.

Hip.—A Thomas's walking calliper splint properly applied will not only mitigate suffering but control or arrest the tendency to bony proliferation. The body weight is transmitted through the tuber ischii and while retaining freedom of movement at the hip joint, the

upward thrust of the head into the acetabulum is avoided and thus mechanical irritation is lessened.

Removal of isolated bony spurs for relief of pain and increase of mobility has been undertaken successfully, but no guarantee of non-recurrence can be given. In inveterate cases excision has been performed, but the results being conflicting, further experience is necessary to estimate its value.

Spa Treatment

The selection of a spa cannot be decided merely on the chemical constitution of the springs, but regard must be had also to climate, altitude, means of access and nature of treatment obtainable, in relation to the vital forces and constitutional peculiarities of the individual.

For combined internal and external application thermal waters are (*ceteris paribus*) most suitable to chronic arthritics. They owe their efficacy to their radium emanations, a portion of which is taken up by the inspired air, while some is absorbed by the stomach and intestines. As they cannot penetrate the epidermis the good effects of baths are attributed to inhalation of the emanations constantly arising from the water. The breathing of an atmosphere containing a certain quantity of emanation is, therefore, extensively practised. To ensure the best effects a *combined bath, drink and inhalation* treatment are advisable. Though further researches are necessary to establish their mode of action, there can be no doubt as to the efficacy of these waters in chronic arthritis. In this country we may allude to the waters of Bath and Buxton, and abroad to those of Wildbad and Gastein.

They are especially suitable for gouty subjects in the middle or later decades of life, also for cases of osteoarthritis and rheumatoid arthritis. In robust plethoric persons of gouty habit and in arthritis complicated by obesity the waters of Harrogate, Llandrindod and similar spas often prove invaluable, those of Llandrindod being preferable in the presence of renal inadequacy by reason of their lower sodium chloride content.

Treatment of Group II

Neuropathic Arthritis. *Charcot's Joints.*—If a positive Wassermann reaction is obtainable antisyphilitic remedies are indicated. In early stages with excessive effusion into the knee or hip, fixation and light weight extension are necessary, followed by aspiration to prevent relaxation of ligaments and capsule. Subsequently, when effusion has disappeared, the joints should be immobilised and relieved of the body weight. In the case of the hip and knee a Thomas's knee-splint may be utilised for this purpose.

Similar measures must be undertaken in the case of the joints of the upper extremities—immobilisation and fixation in the most useful position. By reason of the underlying pathological process, excisions or amputations are inadvisable.

Syringomyelic Arthritis.—Treatment on similar lines to the foregoing is indicated, but owing to the tendency to suppuration in the joints as the result of trophic ulceration in the skin, surgical interference is more often called for. Usually it is for the removal of sequestra, but occasionally amputation is unavoidable.

Hæmophiliac Arthritis.—This may be spontaneous or traumatic in origin; fortunately the patients or their parents are usually alive to their being "bleeders," as death has followed incision of the joint cavity in ignorance of this. In the presence of hæmorrhagic effusion, fixation by a splint and the application of evaporating lotions should first be tried followed by elevation of the limb and firm bandaging if bleeding continues. When the effusion is absorbed, radiant heat or hot-air baths with massage to prevent adhesions are recommended, but all violence is to be deprecated. Chloride and lactate of calcium, also thyreoid and ovarian extracts have been used internally. John has recently recommended the injection of serum or fresh defibrinated blood from a healthy man, and others advise injections of normal horse serum.

Intermittent Hydrarthrosis.—The condition may be associated with a gouty or rheumatic diathesis, arthritis deformans or giant urticaria, and often proves most obstinate.

Of general remedies, iodide of potassium I have found useless, the most reliable drug being arsenic administered over long periods. Quinine and aspirin have also been well spoken of as alternatives. Of local measures rest comes first, and Gordon Watson recommends a rhythmic sinusoidal current (Schnee four-cell bath) during the attack. Hot-air and radiant heat baths have also been used, but the tendency to relapses is very pronounced.

Syphilitic Disease of Joints.—The synovitis of secondary syphilis is sometimes confused with rheumatism, and sometimes with gout, and not infrequently gout and syphilis co-exist. In pure syphilitic forms the internal use of mercury and iodide of potassium combined with local pressure by mercurial plaster often suffices if given a fair trial. Or Scott's ointment may be rubbed into the joints and mercury injected intramuscularly. In the tertiary stage the same general and local treatment is indicated, but surgical interference may be called for in the event of a secondary septic arthritis, or for the removal of diseased bone.

R. L. J. L.

TUBERCULOUS DISEASE OF THE BONES AND JOINTS

Tuberculous disease of the joints, the commonest form of arthritis producing crippling in this country, may attack patients of any age, but especially from the third to the tenth year, though its onset in the second decade is also common.

It is the result of infection by the bacillus of Koch which most commonly obtains ingress through the respiratory or alimentary tracts.

It is seldom if ever inherited, but patients with a bad tuberculous family history are often very susceptible to infection and have diminished power of resistance to attack. The bacillus having entered the body may be sooner or later destroyed without having caused any apparent injury, may remain dormant indefinitely, may cause some slight local lesion which will set up sufficient local reaction to effect its healing, or may produce more or less extensive and active lesions where the patient has low resistance or has had his resistance temporarily lowered by illness or injury. In this way is explained the frequency with which the onset of tuberculous arthritis follows antecedent disease, such as an infectious fever as measles, or slight injury following a fall or blow. Severe injury rarely precedes local infection because the extreme reaction resulting affords adequate protection.

The infection may be caused by either the human or bovine type of tubercle bacillus. Much evidence has accumulated which points to the latter being relatively commoner in joint than in lung infections, though the proportion of joint cases infected by either type is still a matter of dispute.

A primary lesion may occur in any bone or joint, but there are certain well-recognised situations selected while other regions are so infrequently attacked that their involvement constitutes surgical rarities.

Out of 1000 consecutive children below the age of twelve years, suffering from tuberculous disease, admitted to the Cripples' Hospital at Alton, the lesions were as follows—

Spine	415
Hip	330
Knee	145
Ankle	39
Multiple	17
Other	54

It should be mentioned that the patients are classified according to their principal lesion. A very large number have multiple lesions, but these are called cases of "multiple tubercle" only when occurring simply in the smaller joints, and not affecting the spine, hip or knee. For example, a patient with tuberculous disease of the spine, hip and knee would be entered as tuberculous disease of the spine.

It should ever be borne in mind that patients may be long infected before definite lesions can be clinically demonstrated. In many such infection may be suspected by vague and often indefinite symptoms such as slight cachexia, lassitude, malaise followed by wasting, slight fever, and occasionally ill-defined manifestations which may take the form of phlyctenular conjunctivitis, rhinitis and skin eruptions. The reactions of such individuals to tuberculin tests, subcutaneous, Calmette's or Von Pirquet's, will often confirm such suspicion, and wise treatment, when applicable, will save many patients from acute local lesions which may be imminent if active measures to prevent their onset be not at once applied. The value of early diagnosis of this so-called "pre-tubercular" state (which is especially common in children of tuberculous stock) cannot be sufficiently emphasised. The treatment indicated is largely general. Where possible the patient should be removed to a bracing and sunny climate. He should live as much as possible in the open air amidst cheerful surroundings. Regular exercise, but avoidance of fatigue, and ample rest should be enjoined. The diet should be varied but plain, wholesome, attractive and easily digestible. The clothing should be light but warm. The skin should be stimulated by baths and friction, and in short all those measures which will improve the general health and increase the resistance should be enforced. For the slight local manifestations which have been already alluded to appropriate remedies should be prescribed.

In addition, especial care must be taken to prevent the possibility of further infection for such patients as are peculiarly susceptible.

From the foregoing it may be already inferred that the writer strongly holds the view that a local tuberculous lesion is simply a manifestation of a general tuberculous infection. Evidence in support of this view has accumulated rapidly of late years, and indeed it has been claimed by some observers that in all cases of tuberculous disease tubercle bacilli may be isolated from the blood. Further, it may be asserted that the gravest forms of bone and joint and indeed of other forms of tuberculosis are not necessarily those with extensive lesions, but those where there is abundant clinical evidence of severe general toxæmia.

If then tuberculous arthritis or osteitis is a general disease in which arthritis or osteitis are but local manifestations, it must be a first and obvious principle to emphasise the necessity of general as well as of local treatment. All measures should be adopted which will improve

the patient's general health and increase his powers of resistance.

I propose therefore to discuss the treatment of tuberculosis of the bones and joints under the following headings—

1. General and adjuvant.
2. Special local treatment of particular lesions.
3. Treatment of complicating abscesses and sinuses.

(1) General Treatment

The requirements of general treatment may be considered under the following headings—

(*a*) Climatic.
(*b*) Hygienic.
(*c*) Disciplinary.
(*d*) Dietetic.
(*e*) Drug.

Climatic.—Mountain, country, or sea air is indicated. Mountain Sanatoria for surgical tuberculous patients are almost out of the question in this country because the mountain climate, although ideal for treatment, is unobtainable in Great Britain. Our mountains are too enshrouded in cloud and fog, the rainfall is excessive, the amount of sunshine too limited, the extremes of temperature too severe.

Suitable treatment, then, in England can be best obtained at the seaside or in the country.

Speaking generally, I believe that country treatment is better for the early, and sea air for the more advanced or chronic cases, including those with old sinuses. To this rule, however, there would be exceptions.

The patient should be reasonably remote from a town in a district where tuberculous disease is known to be little prevalent. If in the country he should be at a fair elevation, preferably on the slope of a hill facing south so as to secure the maximum sunshine. A sheltered situation is not a necessity, wind is no disadvantage, on the contrary, it exercises a bracing and stimulating effect. The district should be sunny, the rainfall not excessive, and the soil porous and one which quickly dries after the rain. The patient should, therefore, not be in the neighbourhood of a river or in a swampy district where the air is excessively humid. Sudden extremes of temperature are undesirable.

If marine treatment is employed it is desirable that the patient should if possible be remote from a town. A seaside pleasure resort is therefore contra-indicated because here, even though the climate of the district may be excellent, the presence of excursionists and others robs the patient of what at the seaside is a prime necessity—untrammelled use of the beach.

A model marine resort is Berck-sur-Mer in France. The industry of this town may be said to be the treatment of patients suffering from surgical tuberculous affections. They have the unrestricted use of the immense and magnificent beach.

A marine hospital should abut on the sea and face the sun and prevailing wind to derive maximum benefit from all three. There should be an extensive beach of firm sand on to which the patients may be wheeled or may walk unhindered by the pleasure-seeker. A low exposed littoral is to be preferred to a tree-covered sheltered one, and there should in addition be an extensive area of foreshore over which the tide advances or recedes within wide limits. The prevailing wind, blowing over such a beach, becomes charged with substances which exercise a markedly stimulating effect on the patient. Sea, sea-breeze and sun are adjuncts to the cure which cannot be neglected.

Invigorating country and sea breezes in a sunny district exercise a marked effect in improving the appetite and general condition of immobile and recumbent patients which should not be overlooked.

The best results would, in my opinion, be obtained by treatment in two institutions, or one institution with a branch hospital—the one in the country, the other at the seaside—both hospitals under the same management, so that a continuity of treatment could be assured. It should be possible to transfer patients from one hospital to the other so that the benefits of change of air and sea could be obtained. A case which is at a standstill or going slightly backwards could then receive the added stimulus which would often lead to cure.

Hygienic.—The value of abundant fresh air in the treatment of tuberculous disease is so well recognised that it need not be laboured here. The patient should practically live in the open-air, but yet remain sheltered from rain and snow.

That bodily attention which can only be obtained by the best nursing may be included under this heading. The skin of patients, immobilised in the ways indicated for the treatment of tuberculous arthritis, requires the most careful attention to prevent the formation of sores. The skin should be frequently washed and, with due precautions, stimulated by friction. Sea-water baths, when obtainable, are of especial value particularly where chronic sinuses complicate the disease. Indeed, in no class of patients is the necessity of that extreme personal attention which may be summed up under the heading of personal hygiene so necessary as in the tuberculous. The patient should be warmly but lightly clad. Dust must be rigorously excluded.

Disciplinary.—Patients accepted for treatment for long periods in large institutions need

kind but firm and tactful handling and occupation suited to their limitations, unless they are to lose that mental distraction which is a powerful aid to cure. Moreover, if left without occupation they may become discontented and degenerate. Children should be educated, adolescents trained and adults occupied according to their capabilities.

Dietetic.—A liberal, plain, varied, easily digested and assimilated diet suited to the somewhat capricious appetite of the tuberculous should be prescribed. Milk and meat should play a plentiful but properly proportioned part in the dietary. The necessity for individualisation where possible is emphasised. Special dietaries prescribed therapeutically have been described. Of these, perhaps the most interesting is that due to the researches of Ferrier. This dietary is based on the observation that healed tuberculous lesions are found post-mortem to be calcified, and on the assumption that tuberculous lesions are spontaneously so healed. Ferrier endeavours to assist this natural calcification by dietetic measures and claims to have successfully achieved his purpose by observing the following rules : Avoid acids and acid fermentation in the intestinal tract because this promotes decalcification. Avoid also alcohol, salads, sauces, oranges and lemons, butter and reduce starches. Drink alkaline fluids freely, especially St. Galmier and Vichy waters. Enjoin a sparse and fat free diet. Prescribe the following cachet—

Carbonate of lime gr. viii
Tri-basic Phosphate of Lime gr. iii
Sodium Chloride gr. ii ss
Calcined Magnesia gr. i.
Thrice daily for adults.

Drug Treatment.—Drugs in tuberculous arthritis have as yet limited application, but used wisely may materially assist in treatment. They may be divided into two classes—general and specific.

General.—Of these the most important are suitable aperients where required. The avoidance of intestinal stagnation has been vigorously advocated by Arbuthnot Lane and others. The slight anæmia often associated with tuberculous arthritis may be treated with arsenic and organic salts of iron, but until the progress of the disease is arrested these have little effect.

Stimulants and tonics are sometimes of value, particularly when the patient, while not actually becoming worse, appears to be making no headway against the disease.

Cod-liver oil is by some regarded as almost a specific. If tolerated by the patient it may be advantageously prescribed, but its value has in my experience been greatly overrated.

Specific.—These constitute both the hope and despair of the therapist. The value of tuberculin is still uncertain. On the whole, more experts in the treatment of surgical tuberculosis deprecate than advocate its employment. Few therapeutic measures have aroused more controversy or such divergent opinions. At present each practitioner must draw his own conclusions—either from the lessons derived from his own practice or the advice he cares to take from those specially qualified to express an opinion.

Briefly and dogmatically, I would make the following statements as representing my present views.

Do not employ tuberculin in cases which are doing well without it. If the patient is not making satisfactory progress endeavour to ascertain the cause and where possible rectify it. For example, try climatic change, altered dietary, improved orthopœdic measures, etc., which may alone be sufficient. If every possible means of assisting the patient has been unsuccessfully attempted the patient should certainly be given the chance of any assistance which the administration of tuberculin might offer. I have not been able to convince myself that small carefully graduated doses of tuberculin have caused immediate harm. On occasions I have seen patients so treated with tuberculin improve remarkably, but, on the other hand, I have observed similar patients improve equally without its aid and indeed without apparent cause. Tuberculin, if used, should be administered subcutaneously, or on occasions intrafocally. It is best to avoid temperature reaction. Its administration is most scientifically graduated if governed by observations of the opsonic index as advocated by Sir Almroth Wright.

It would appear to be especially indicated in patients with a consistently abnormal opsonic index who are otherwise being treated correctly, particularly in cases with evidence of a general toxæmia as shown by absence of reaction to treatment or to the progress of the disease, absence of muscular spasm, cachexia, etc. Properly administered, it is undoubtedly of value in controlling the opsonic index when auto-inoculation or other conditions affecting the index are present, but it cannot be accepted as satisfactorily demonstrated that the index is a reliable guide to treatment.

If tuberculin is employed the varieties known as Bacillary Emulsion (B.E.), Beraneck's tuberculin or Rosenbach's tuberculin are suggested.

For details as to the safe employment of tuberculin reference should be made to standard authorities.

Vaccines may be employed in the treatment of septic sinuses complicating tuberculous

lesions. The common added infections are staphylococci, streptococci, B. coli, B. pyocyaneus and diphtheroid organisms.

The former is most frequently found. Autogenous vaccines are most usefully employed when the sinus first becomes infected. In chronic sinuses stock vaccines may be used to increase the flow of discharge which sometimes has a mechanical value in cleaning the part infected. Vaccines very rarely will of themselves cause a sinus to heal. Vaccine treatment is sometimes of value preparatory to bismuth treatment (to be later described).

Serum-therapy in the hands of the author has been of so little service that he would simply allude to the work of Marmorek and Spengler if further information in this branch of specific treatment is desired.

Chemiotherapy.—The work of Ehrlich in the treatment of syphilis has stimulated research in this method of treatment. Some German investigators have been using copper salts combined with methylene blue or with lecithin derivatives. Their researches are promising, but the work is still so experimental that it cannot be more than alluded to here.

Minchin strongly advocates the employment of garlic both internally and in the form of an ointment, especially where sinuses are present. Trial of this treatment at Alton has been disappointing.

Pneumosan and dioradin are proprietary drugs advocated by some.

Adjuvants.—Under this heading may be included such aids to treatment as sunlight, X-rays and Bier's hyperæmia—methods which, while not only applicable to the treatment of tuberculous bone and joint disease, are yet of especial assistance in these conditions.

Attention has been prominently attracted recently to the value of heliotherapy especially through the writings of Rollier of Leysin, who has achieved brilliant results by its aid. He is particularly enthusiastic as to its utility, but while sun treatment is undoubtedly of the greatest assistance, the success Rollier has achieved is probably in a large measure due to the fact that his treatment is essentially conservative. Sun treatment may be adopted in any sunny locality. It is best obtained where there is abundant sunshine of high actinic power. In mountainous districts free from mists, with clear air and wide expanses of snow, the actinic power of the sun is especially high, and here heliotherapy can be practised to greatest advantage.

Rollier recommends individual treatment gradually applied with especial reference to the idiosyncrasy of each patient. At first the patient should be gradually exposed to the sun, and only after some days should complete exposure be attempted. Eventually, the patient, wearing only bathing drawers and a large hat, may be exposed to the full rays of the sun for prolonged periods. This gradual exposure prevents syncope or blistering. The skin gradually assumes a beautiful bronze tint. The pigmentation varies with the power of resistance. Delay in its appearance is a bad prognostic sign. Indeed, I have observed some patients with marked cachexia and suffering from obvious toxæmia in whom the most prolonged exposure to the sun will not produce a healthy pigmentation, and these cases are invariably serious. The effect of sun treatment on sinuses is sometimes especially marked—discharge rapidly dries up and healthy cicatrisation is common. Sequestra are sometimes spontaneously expelled. Joints affected often recover their mobility to a remarkable degree.

X-ray therapy and Bier's treatment is dealt with elsewhere.

(2) Special Local Treatment of Particular Lesions

Spinal Caries. *Treatment* may be directed to: (1) the improvement of the general health of the patient and increase of his powers of resistance; (2) to heal the local lesion; and (3) to prevent or correct deformity.

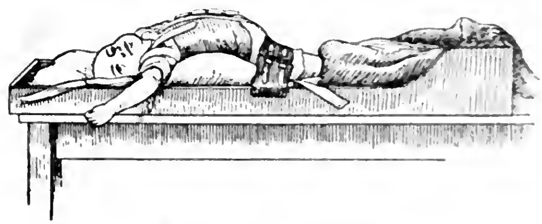


Fig. 1.—Spinal Board

In active spinal caries it is essential that general rest should be enforced, and absolute rest of the affected part is desirable. Muscular spasm must be overcome, and it is desirable that the patient should be kept recumbent, immobilised in the region of the lesion and hyper-extended—the hyper-extension being designed to overcome muscular spasm and to prevent the onset of deformity. In cases where there is marked spasm the hyper-extension should be aided by traction extension. Numerous appliances have been recommended at this stage of the disease. In England the common form of apparatus still employed is the Phelp's Box. In America the Bradford frame is more usually used and is indeed much to be preferred, but for convenience in nursing and efficiency in treatment few forms of apparatus can excel the spinal board as used at the Hôpital Maritime, Berck-sur-Mer, and this will be fully described.

The board is an oblong tray made of strong but light wood, the length should be from 12 in. to 18 in. more than the patient's length and the width about 8 in. greater than his greatest width. The sides and ends of the board should be 4 in. high with the exception of the foot-end, which is raised to a height of 18 in. so as to take away from the patient's feet the weight of the bedclothes and prevent the onset of foot-drop. The bottom of the board is perforated with numerous holes to allow for free ventilation of the overlying mattress. The corners of the board are bound with sheet-iron angle pieces which will add greatly to the strength of the apparatus without unduly increasing its weight. Appropriate handles are attached to the head and foot to facilitate easy transference. In cases of dorsal or lumbar caries there should be placed across the board and underneath the mattress below the region attacked a hard pillow, which will hyper-extend the spine. The pressure on the spine

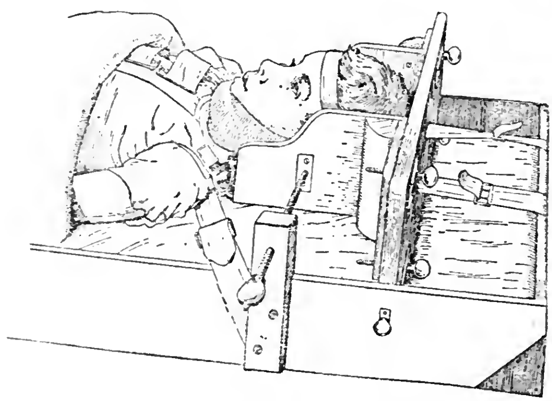


Fig. 2.—Adjustable Box-splint Head-piece.

thus produced will prevent deformity or tend to correct deformity if already existing providing the lesion is not of too long-standing and ankylosis has not occurred. The mattress should be of well-prepared horsehair. The patient is fixed to the board by a jacket composed of stout jean fitted accurately to the trunk and stiffened laterally with whalebone to prevent rucking. At the back of the jacket two straps of webbing are let in which cross each other in the form of a St. Andrew's Cross, and these are buckled to the sides of the board to prevent the patient moving in any direction and to keep him in the position of selection. This jacket should be laced or buckled over the front of the patient, This board has numerous advantages. It is simple, efficient, portable, convenient for nursing, hygienic and comfortable. The bed-pan can be easily administered by merely slightly raising the buttocks, and when the disease is less acute the board may be safely tilted to a limited extent for the greater comfort of the patient.

In cases of cervical caries, the board, with a head-piece, as illustrated, is desirable. This is attached to the head-end of the board and so adjusted that the patient's head is kept immobile. Very slight hyper-extension is all that is required in these cases, but head-extension is usually desirable. This head-extension may be applied by a leather chin strap and occipital band which should meet just above the ear. At their junction attached webbing passes through slits in the headpiece and is buckled to elastic bands which may be tightened to any degree required, consistent with the patient's comfort, and forms an efficient and suitable extension. The jacket, already described, fixes the trunk and forms an admirable means of counter-extension. This method of immobilising the head is much to be preferred to the sandbags commonly used, which are constantly being displaced and are therefore inefficient. While the apparatus just described is admirably useful and very efficient, yet when skilled nursing is obtainable better results still may be obtained by the adoption in suitable cases of selected varieties of the "backdoor" splint.

Measurement of the Splint.—A large sheet of paper is placed on an ordinary table and the patient stretched thereon on his back. On this paper the outline of the trunk is then traced. The splint may be a shade smaller than the contour of the trunk. A piece of well-seasoned beech wood $\frac{3}{4}$ in. in thickness is cut to exactly the shape and size of the tracing thus made. The outer part of this is cut away 1 in. from the periphery all round, forming an outer frame. This is covered with lacquered sheet iron and forms a strong and rigid framework. The inner part or backdoor is pared down so that it can be inserted or removed with ease and both the backdoor and frame are suitably padded. The backdoor is held in the outer frame by clips. The outer frame is mounted on legs of convenient height and suitable support made for the head and legs of the patient. Straps attached to the outer frame fix the patient.

The nature of this splint and the way it is used are most easily understood by reference to the illustration.

In cases where there is marked psoas spasm or psoas abscess the legs may be strapped to a back splint hinged to the outer frame which will keep the psoas muscles stretched and at rest. Foot-pieces may be added to prevent the weight of the bedclothes pressing unduly on the feet.

It will be seen that a patient treated on this contrivance is accurately immobilised in the position of selection. The backdoor can

easily be inserted or removed without even turning the patient and is padded to the exact degree required to secure the proper hyper-extension of the spine. The padding should be of animal wool, as this is springy, elastic, comfortable and lasting. The backdoor should be removed at frequent intervals for inspection and cleaning of the back and to prevent possible formation of sores. A patient on such a splint can be safely nursed providing he has a skilled attendant and the surgeon is assured that there can be no mistake in the readjustment of the patient after the necessary attention has been given to the spine. Where there is much spasm, head and pelvic extension may in addition be employed, but this is rarely required. Contrary to what might be expected, this splint is perfectly comfortable. From a somewhat extensive experience I have on no occasion seen it objected to by any patient.

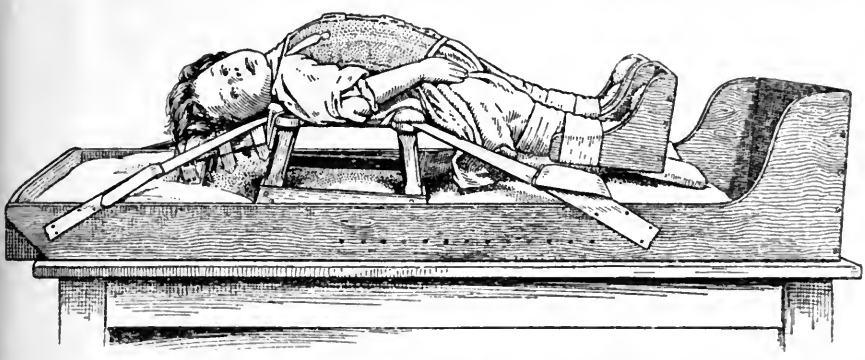


Fig. 3.—Patient suffering from Spinal Caries on a "Wheel-barrow" splint. This splint is specially indicated in cases where psoas spasm or psoas abscess complicates the disease. A removable and suitably padded back-door is placed under the patient which hyperextends the spine to any degree desired and gives facilities for care to the back and inspection of deformity without removing the child from the splint. Foot-pieces are incorporated to prevent any danger of foot-drop.

The length of time recumbency and hyper-extension should be ordered varies considerably with the case being treated. In early cases it is usually sufficient to keep a patient in this attitude until all muscular spasm has disappeared provided then the patient's general condition is satisfactory.

It should again be emphasised that there is a certain type of patient in whom little spasm manifests itself and little deformity arises, but in whom general symptoms of tuberculous infection are marked, and these should be kept recumbent for a very prolonged period under the best hygienic conditions until the improvement in general health justifies abandoning the recumbent attitude. In cases where deformity exists, as much deformity as possible should be corrected while the patient is recumbent, and this may necessitate prolonged treatment in this attitude. In no cases can a fixed rule be made as to when the patient should be allowed to leave the horizontal position, and decision on this point can only be arrived at after consideration of the whole facts of each individual case. Commonly, recumbency from three months to a year is required. In some cases recumbency must be prolonged for a very much greater period, particularly in the case of a lesion high up in the spine. It may be taken as a general working rule that the higher in the spine the lesion is the longer recumbency will be required and the more grave will be the prognosis. Cervico-dorsal or cervical cases, indeed, especially where paraplegia complicates the condition, form by far the most difficult class to treat. When recumbency has been sufficiently long enforced the patient may be gradually tilted on the spinal board already described until he can assume the erect attitude with safety. This is effected by gradually tilting the board to a more nearly erect position for a short time daily, and commonly at the end of a fortnight the patient may be safely placed vertically without any sign of faintness.

When this has been achieved it is desirable to adopt some other means of support to the spine, and for this purpose nothing is more satisfactory than a carefully applied plaster of Paris jacket. Plaster of Paris may be applied to the spine when the patient is in the horizontal position or suspended, and the latter method is usually to be preferred, particularly if the lesion is above the dorso-lumbar region. For two days previous to the application of the jacket the patient should be carefully dieted. Milk, vegetables and foods likely to cause flatulence should be avoided, the bowels thoroughly cleared and the patient suspended on suitable gallows, care being taken that he is placed in the best attitude possible. This is secured by careful application of the suspending bridle, which should be so attached that the spine is hyper-extended to the degree required. Slight hyper-extension is usually desirable, and care should be taken that if there is any deformity any compensatory lumbar curve below the deformity is largely obliterated. A well-fitting cotton vest turned inside out is put next to the patient's skin, and on to that the plaster of Paris jacket is applied. The jacket

should be made with plaster bandages from 4 in. to 6 in. wide. The bandages should be placed in cold water, as the resulting set is better than if placed in warm water. The bandage should begin below the right iliac crest and be wound round and round the trunk from below upwards, a pleat being made in each circle of the trunk so that there is no undue constriction and so that the jacket when completed shall allow the trunk to enlarge to its maximum capacity. The jacket must be

Fig. 4.—A skeleton in a plaster-of-Paris jacket as used for cases of cervical and cervico-dorsal caries. Note the moulding round the pelvic brim, the clavicles, the mastoids and occiput. The weight of the head is taken off the spine and movements of the head are prevented by the fillet around the forehead, which keeps the head immobile but allows free movements of the jaws.

very carefully moulded round the whole of the pelvic brim, sacrum, iliac crests and pubis, for from the fixed pelvic base all the support is obtained. The shoulders should be depressed and the jacket carefully moulded along the clavicles. In this way there will be no possibility of flexion of the spine and there can be no increase of any existing deformity. In cervical cases, the plaster will have to encircle, in the first place, the whole of the head, leaving exposed only the eyes, nose and mouth. The plaster must be carefully moulded on to the occiput and both mastoids. Subsequently all unnecessary parts of the jacket are removed. Unless considerable experience has been acquired in the application of plaster jackets, plaster is not recommended in cervical cases because of the difficulties of its application to any but an expert, though in expert hands no form of support is more efficient. After the jacket has been applied, and has well set, a large ventral window is cut out from the middle of the sternum above to the region of the umbilicus below. This large window will not interfere with the support the jacket should give, but will yet allow ample space for respiration and digestion and will immensely increase the comfort of the patient. All unnecessary parts of the jacket are removed, and it is finished off by the edges of the subjacent vest being turned over the edges of the cut plaster and fixed to the jacket by plaster cream. In such a jacket a patient may remain for many months with perfect comfort and adequate support. Plaster of Paris has the added advantage of being porous and when properly applied is not harmful to the subjacent skin. The patient is left in this apparatus until there is reasonable evidence of the lesion having firmly consolidated. Sometimes it may be necessary to repeat its application and keep the patient in such a support for possibly a year or longer. When it has been decided that the plaster jacket may be safely discarded some other form of support —this time a removable apparatus—should be substituted and should be worn at all times except when the patient is in bed.

Many forms of removable spinal jackets have been advocated. Of these the most popular at present in this country is the poroplastic jacket, which is only alluded to here to be condemned. Well-made and properly designed steel braces are more serviceable, but the neatest, most efficient, lightest and most comfortable support that can be applied is the celluloid splint, which has been recently introduced.

The Manufacture of a Celluloid Jacket.—The patient is again suspended on the gallows and his naked trunk oiled. On to the trunk a new plaster-of-Paris jacket is quickly applied, the plaster bandages being this time soaked in warm water, for the patient's greater comfort. As soon as the jacket is set it is removed from the patient by making an incision on one side of the trunk. The jacket is then mended and all except the part where the neck projects covered with plaster bandages suitably applied. The inside of this negative is well greased and into it is poured cheap fluid plaster of Paris. When this has set the negative is removed from the positive, which now forms an exact replica of the patient's trunk. This positive may be

advantageously moulded with a knife to accentuate the pelvic brim, which will afford purchase for the jacket about to be made. A vest is then carefully applied to the positive, and on it is painted a solution of non-inflammable celluloid. After this a layer of muslin is applied, which is again painted with fluid celluloid, and the process repeated until the necessary strength is obtained. Between each application of the celluloid solution sufficient time should be allowed for the acetone to evaporate and leave the dry celluloid thoroughly impregnated into the vest or muslin. When a sufficient thickness has been attained the jacket should be removed from the cast by a longitudinal cut down the middle in front and tried on the patient. All unnecessary parts of the jacket are then marked out for removal and again a large ventral window is made. The edges of the jacket are then finished off by being bound with leather and arrangements are made to lace the jacket up in the front. If necessary, its strength may be further increased by reinforcement with duralumin. Such a jacket admirably serves for support of the spine when a patient is convalescent. It is so light that its presence is hardly recognised, but yet it affords all the support required. It should be worn for a year or two until support for the spine has become unnecessary.

Radical Treatment of Spinal Caries.—Many surgeons still advocate operative measures when abscesses complicate tuberculous disease of the spine, but given adequate facilities for the conservative treatment of patients such measures should be condemned. Incision of a psoas abscess, no matter how carefully performed, results only too frequently in eventual sinus formation, and abscesses which are at all accessible to the knife can be much more safely evacuated by aspiration.

In long-standing cases of paraplegia, laminectomy may be indicated, but this operation should not be lightly undertaken as the prognosis is not favourable. Costo-transversectomy is sometimes indicated when a mediastinal abscess exists which, increasing in size, causes dangerous symptoms, but I have rarely found this operation necessary. For the description of technique to be adopted reference should be made to the standard books on surgery.

One operation which has lately come into prominence—that advocated by Albee—may be here mentioned. It is really in the nature of a conservative measure. Albee recommends that in cases of lumbar or dorsal caries the exact site of the lesion should be carefully ascertained by X-ray examination. This having been done, a semicircular skin flap is dissected back over the lesion and the spinous processes exposed—the semicircular flap should extend well above and below the part affected. The spinous processes are carefully split. One of the patient's legs is then bent back on to his thigh and a suitable strip of the tibia of the necessary length cut out with a specially designed motor saw. This strip of tibia is inserted between the split spinous processes and should extend from two vertebræ above the lesion and two vertebræ below, where this is possible. The graft is held in position by kangaroo tendons, and in the course of six or eight weeks is said to be incorporated with the spinous processes and thus acts as a very efficient internal splint. After the operation, the patient is kept in a recumbent position for three months, and may then, if he has made satisfactory progress, be allowed to walk about with or without any spinal support. The operation is an ingenious one, and in my opinion it is especially indicated in adults where prolonged recumbent treatment is a serious drawback, but the exceedingly good results obtainable by less drastic conservative measures renders it undesirable in children, if reasonable facilities are obtainable for their treatment. Complications have already been reported as a sequel to this operation, and while much may be expected from it it should not be lightly undertaken.

(For conservative treatment of abscesses and sinuses, see below.)

Hip Disease. Treatment.—In the acute stage complete recumbency should undoubtedly be advocated. Deformity may be prevented, or, if not associated with ankylosis, usually corrected and pain relieved by the application of suitable extension to the affected limb. The method recommended is that advised by Professor Howard Marsh. The patient is treated in a recumbent position on a firm mattress and a Liston long splint is applied to the sound side. Extension is applied to the diseased hip, bearing in mind the following rule: *Lordosis if present must be corrected by flexing the affected limb until the spine is flat upon the bed. The anterior superior iliac spines must then be so adjusted that they are on the same horizontal plane and the straight line joining them is at right angles to the long axis of the trunk.* Extension applied to the affected femur in the direction the leg now occupies will act effectively. The object of this extension is to counteract the effect of existing muscular spasm, correct or prevent deformity and relieve pain. The weight to be applied, therefore, should be sufficient to achieve this purpose. Commonly, in a child, from three to six pounds will be sufficient. Extension strapping is commonly used. To prevent foot-drop the strapping may be usefully attached to the foot splint here figured, which was first introduced

at the Maritime Hospital, Berck-sur-Mer. This contrivance also has the advantage of lessening the liability to the formation of heel-sores, preventing foot-drop and reducing the risk of eversion or inversion of the foot. Better still, however, is the employment of plaster extension. The foot being flexed at right angles to the leg, plaster bandages are applied from the toes to midway between the condyles of the femur and the great trochanter. Incorporated laterally with this plaster are two pieces of stout calico bandage which are attached to a stirrup below the foot, and from this stirrup the extension cord extends in the line of the femur to a suitably placed pulley at the bottom of the bed. The plaster must be moulded most carefully around the femoral condyles, as it is from these that the pull is exerted. This

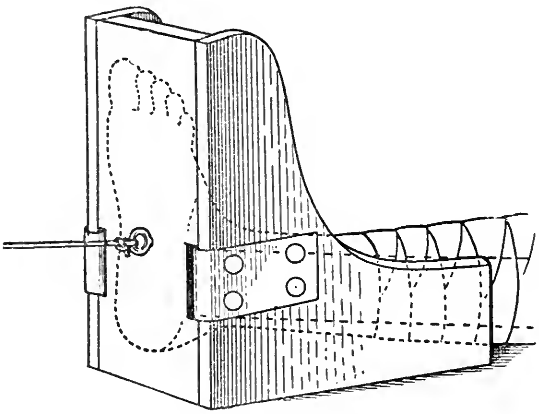


Fig. 5.—Foot-splint for extension.

contrivance has the advantage of simplicity, security, permanent application of the extension weight direct to the affected femur, avoidance of injury to the knee, prevention of foot-drop and avoidance of heel-sores. Moreover, as it practically constitutes a jointless rod from toes to hip it tends itself to the prevention of eversion or inversion up the leg if a strap is pinned into the plaster and so adjusted that steady traction is applied in opposition to the rotating force.

A useful means of rapidly correcting deformity due simply to muscular spasm is afforded by the administration of a general anæsthetic. The limb can then be fixed instantly, painlessly and safely in plaster of Paris in the desired position. Should spasm have been considerable this immobilisation in the position of choice should be associated with extension. The combination may be well effected by applying plaster extension as just described. Around the plaster above the knee-joint wind two or three thicknesses of lint and apply over the lint plaster bandages to fix the hip joint. Subsequently remove the lint and the solution of continuity in the combined plaster, while not sufficient to allow mobility to the hip, is still sufficient to enable extension to be continued. Such a device has been found of the utmost value at Alton. When the acute symptoms have subsided, spasm has been completely overcome, starting cries at night have ceased and deformity is corrected, immobilisation of the affected hip-joint by means of a plaster extending from the ankle to well above the iliac crest is advisable. All plasters applied should be most carefully moulded around the condyles of the femur, under the great trochanter and around the whole of the pelvic brim. The plaster may be well cut away over the abdomen but posteriorly must extend as far inward over the buttock on the affected side as is practicable consistent with cleanliness. Should an abscess or sinus complicate the disease a large window must be cut out in the situation it occupies and the plaster reinforced to maintain its strength. The edges of the window may be painted with shellac to prevent any danger of saturation when there is any discharge.

A short plaster spica about the hip-joint will be sufficient when the diminished activity of the disease allows ambulatory treatment to be undertaken.

Many surgeons employ the Thomas' hip-splint, but the difficulty of obtaining efficient immobility with this apparatus and the extreme liability to eversion or adduction is such that its use is not commended. Given mastery of plaster technique, the splint cannot compare in efficiency with a short or long plaster spica.

During convalescence a celluloid hip-splint is admirable (see celluloid in spinal caries for technique of its manufacture).

For the first six months at least after recumbency is abandoned the patient should walk with the assistance of crutches and with a patten on the sound limb. The periods at which the various stages of the mechanical treatment should be applied will depend on the progress made by the patient, which may vary considerably in different cases.

It may be asserted that recovery of movement at the hip-joint is most likely to occur if prolonged and adequate immobilisation has been insisted upon, and it is extremely gratifying to observe that patients who have been treated from the onset of the illness in the manner suggested usually recover a wide range of movement, without deformity and with very little shortening. (For treatment of abscesses and sinuses, see below.)

Radical treatment is best avoided, and

excision of or amputation at the hip-joint should never be necessary.

In cases of bad flexion and adduction associated with ankylosis sub-trochanteric osteotomy is advocated. Tenotomy of the adductors must often be performed simultaneously.

Tuberculous Disease of both the Hip Joints.—This is fortunately somewhat rare and is a serious condition requiring care and skill in treatment. Inefficiently treated it commonly produces a very distressing deformity due to adduction of both legs and forming what is sometimes called the "scissor-leg condition." It should be treated for a prolonged period in double plaster extension combined with immobilisation, as already described.

Fig. 6.—A patient convalescing from tuberculous disease of the right hip-joint in a celluloid splint.

Sacro-Iliac Disease.—This forms one of the most difficult tuberculous lesions to treat, especially if complicated by abscess or sinus formation, and indeed an intra- or extra-pelvic abscess very frequently forms. The latter may be evacuated by aspiration—the former, if small, and prolonged recumbency is ordered, may absorb, but should it extend, as it usually does, to a point accessible for aspiration—as in one or other of the iliac fossæ—should be evacuated by this means. Very prolonged recumbency is advisable, the pelvis should be immobilised and the legs strapped down. A double hip plaster is often of value. If radical measures are adopted they should aim at the complete extirpation of the local lesion, and extensive operation is essential if good results are to be obtained, but operation is associated with considerable risk.

Tuberculous Disease of the Knee-joint.—This may begin with either synovial or bony infection—the latter being the commoner. The onset is commonly manifested by subacute synovitis, often with effusion and accompanied by some muscular spasm and pain. The knee tends to flex and the tibia may undergo some external rotation and subluxation, thus forming the triple displacement so marked in untreated cases. Very frequently, in early cases, when the disease is osteal, the lesion may be accurately localised by clinical and radiographic examination, and in such cases complete removal by radical measures of the area affected—providing the joint has not been infected—facilitates cure, but great care should be taken to ensure complete removal of the part attacked. Excision of the knee-joint should only be advised in adult cases, and even in these conservative treatment is usually to be preferred. When treated conservatively, rest in bed should at first be enjoined with extension to abolish muscular spasm. Should triple displacement be beginning, extension of the tibia is advocated combined with counter-extension of the femur, which may be sufficiently flexed to allow the tibia to lie parallel with the trunk. In many cases it will be found that the deformity may be most quickly reduced by repeated plaster applications, if necessary under an anæsthetic. Commonly gentle manipulation may be employed and the plaster should extend from the foot to above the pelvis, particular care being taken to mould the plaster around the ischial tuberosity on the affected side. When the knee is straight a well-fitting Thomas' knee-splint properly applied is admirably efficacious and of use in ambulatory treatment. During convalescence a celluloid knee-splint may be usefully employed. Parenchymatous infiltration by iodoform solution is sometimes practised, and Bier's hyperæmic treatment is often of value.

Erasion and scraping operations should not be practised if they can possibly be avoided.

Tuberculous Disease of the Ankle.—In this, early localisation is specially strongly commended. If the astragalus is alone infected astraga-

lectomy is an operation of value when time is of importance, because this operation, skilfully performed, leaves little impairment of the functions of the foot. Scraping operations should always be avoided. If other bones are attacked or the disease is synovial, prolonged immobilisation in plaster with the foot at right angles to the leg is very effectual in treatment. As the disease subsides a well-fitting celluloid splint, with crutches and patten on the sound foot, safely permits early ambulatory treatment.

Bier's hyperæmic treatment is of particular value in these cases.

Tuberculous disease of the bones of the foot not involving the ankle-joint is not uncommon, and early removal of the bone affected may here be undertaken to prevent further spread of the disease, or conservative measures may be adopted.

Tuberculous disease of the upper extremities is relatively uncommon. In all the joints of the upper extremity Bier's treatment is often of value. In the shoulder, onset may be especially rapid, and here early operative measures, particularly in adults, are sometimes of value, particularly if the disease is very localised. Otherwise, the joint should be immobilised in plaster of Paris with the arm fully abducted in case ankylosis should ensue. If thus immobilised a window should be cut in the plaster over the joint to permit its repeated examination, and if an abscess forms this should be aspirated.

Tuberculous disease of the elbow in adults is perhaps best treated by early excision. In children fixation in plaster is to be preferred—the elbow being flexed to a little less than a right angle with the thumb pointing upward.

In the wrist-joint, swelling, rigidity, muscular wasting, sometimes palmar displacement, pain and tenderness are indications of the disease. Early plaster fixation and gradual correction of any deformity which may exist is to be advised. Excision of the wrist-joint should rarely be advocated.

Tuberculous Dactylitis.—This is commonly associated with tuberculous disease elsewhere—not infrequently in the spine. The disease is here usually in the nature of osteomyelitis. Fixation in plaster is usually sufficient to procure relief, even when abscesses are present, but occasionally the bone must be incised and the caseous material evacuated. Subsequently, sun or X-ray treatment is usually then of value.

(3) Treatment of Complicating Abscesses and Sinuses.

The commonest complication directly associated with tuberculous arthritis is abscess formation and the most serious the formation of sinuses. The formation of an abscess is not altogether to be deplored, and in fact in many cases, if the abscess can be safely evacuated, its formation is advantageous. Generally speaking, evacuation of an abscess by aspiration is recommended and occasionally when an abscess is small and easily accessible, it—together with the lesion from which it has originated—may be completely excised, and such treatment is at times desirable. An abscess in an inaccessible position, such as one in the posterior mediastinum, occasionally requires evacuation by ordinary surgical means. In these cases, by the aid of the operation of costo-transversectomy, but in the majority of cases, if the abscess is at all accessible, aspiration is the best means of treatment, and incision should be avoided.

Abscesses should be aspirated with a suitable trocar, cannula and syringe through as much healthy tissue as possible. The trocar should enter, where possible, on that side of the abscess where the abscess is least likely to extend. Abscesses associated with the hip-joint usually track down the limb, and the trocar should enter, where possible, on the trunk side, as they are least likely to extend in this direction. A psoas abscess should be entered in the region of the corresponding anterior superior iliac spine. The skin should be pulled towards the umbilicus and the trocar inserted around the curve of the iliac crest. When the trocar is withdrawn the skin sliding back into its original position will form a valvular seal to the orifice made by the needle.

Should the pus be fluid, complete evacuation is possible with one aspiration, but the pus may rapidly re-collect and in that case repeated aspiration may be required—commonly three or four aspirations are sufficient, but many more may be necessary. That numerous aspirations may be required is by no means a contra-indication to this method of treatment, but rather emphasises its necessity, for if abscesses requiring repeated aspiration are incised the pus will equally certainly re-collect and sinus formation result. If the pus is very fluid and the abscess thin-walled, injection of a 10 per cent. solution of sterile iodoform in sulphuric ether has a drying and sclerosing effect. It promotes formation of new fibrous tissue in the abscess wall which retracts and thickens the wall and so hastens the cure of the abscess. The ether should be allowed to escape in gaseous form through the cannula, leaving freshly precipitated iodoform on the abscess wall. The quantity of the solution to be injected should rarely exceed ten cubic centimetres. If the tissue about the abscess is infiltrated and the pus is of a somewhat fluid consistency a combined iodoform solution of the following formula is recommended—

Iodoform gm. 5
Ether gm. 10
Guaiacol and Creosote gm. 2 of each
Sterilised Olive Oil 100 c.c.
Dose 5 to 10 c.c.

Should the pus be caseous its liquefaction will be aided by the injection of the following solution—

Thymol 1 part
Camphor 2 parts
Sulphuric Ether 3 parts
Dose 2 to 5 c.c.

The former dose should first be employed—the larger may be used in very intractable thick-walled abscesses. The action of this solution is physiological. It promotes the invasion of the abscess with leucocytes, the ferment of which digests and liquefies the caseous pus and necrotic material.

The treatment of infected sinuses associated with surgical tuberculous lesions is still unsatisfactory. Sun treatment is often of value when obtainable. Sea-water baths are occasionally of considerable assistance, and climatic change may afford great aid. When due to an accessible sequestrum this sequestrum should be removed. Often adequate plugging by gauze or alteration in the position of the patient to facilitate drainage is of value. In some cases, particularly in hip disease where there is no temperature, patients with sinuses who have been recumbent may often be greatly benefited by being allowed to abandon recumbency and enjoy gentle walking exercises. Should the sinus become obstructed and tend to burrow into neighbouring tissues it should be freely laid open, but scraping operations are not commended.

Prominent among recent measures introduced for the cure of sinuses is the employment of Beck's bismuth paste. This is especially valuable in very old sinuses when not associated with amyloid disease—particularly if the bony lesion is healed but the sinus persists. Pure sterile bismuth sub-nitrate mixed with two parts of sterile vaseline heated to the temperature of the body and injected into a sinus often has a remarkable effect in procuring speedy healing. By some bismuth carbonate has been preferred to bismuth sub-nitrate on account of the alleged toxicity of the latter salt, but I have found the sub-nitrate of greater therapeutic value. In cases where increased discharge from the sinus is desired, Sir Almroth Wright has advocated the injection of the sinus with citrated hyper-tonic solution of the following formula—

Sodium Chloride 2 parts
Sodium Citrate 1 part
Dissolved in boiling water (100 parts)

and he also advocated the administration of sodium citrate by the mouth.

Where sinuses have been recently infected the use of autogenous vaccines is indicated, and is often associated with rapid amelioration. X-ray treatment is also of great value in certain cases, particularly on ulcerated surfaces. H. J. G.

TREATMENT OF SPRAINS AND OTHER INJURIES ABOUT JOINTS

The following article outlines briefly a method of treatment for sprains and allied injuries about joints by graduated contraction of the muscles.

The contractions are produced by stimulation with an induced current, and as far as this is concerned the method is an electrical one, but the electricity itself is not the curative factor.

It is simply the stimulus, and it is the contraction of the muscle, with the attendant circulatory and chemical changes, which produces the desired result.

The apparatus used is simple. It consists of a specially wound small induction coil actuated by a dry cell. The secondary (induced) current is used, and the intensity of the stimulus is controlled by inserting or withdrawing the soft iron core in the primary coil.

The contraction produced in the muscle may be minimal, submaximal, or maximal, according to the wish of the operator, and both the amount of contraction and the rapidity with which successive contractions take place are under his absolute control.

The contraction is gradual, rising slowly to the desired maximum and falling equally gradually. There is no shock and no local tetanus under the electrode, but rather a slow uniform contraction of the whole muscle from origin to insertion.

This type of contraction is essential, and a series of faradic shocks each of which of course produces a single contraction, does not have the same effect clinically on the muscle.

The voluntary contraction of muscle is perfectly imitated, and on looking at the treatment taking place, it appears as though the patient was moving the joint voluntarily, whilst actually it is the rhythmic contraction and relaxation of the controlling muscles, stimulated by the coil, which are producing the movement.

A strained muscle is damaged to an extent depending on the severity of the injury, and its tone is either partially or wholly lost in consequence. What is claimed is that the restoration of the muscle tone—the essential factor to recovery—is brought about more quickly by this method of electrical stimulation than by any other. The temporary recovery

of tone is immediate, and although only temporary at first, the effect after each treatment lasts for a longer and longer time.

The patient cannot fail to be conscious of this improvement; he begins to use the limb, and so by active exercise, only made possible by this temporary restoration of tone, hastens his own cure.

And here let it be stated that rest has no part in the treatment of sprains, after the first twenty-four hours. Again the treatment by strapping or firm bandaging, advocated by some authors, is, if this method of treatment by graduated contraction be adopted, not only unnecessary, but actually harmful and retards progress.

The supporting material must, if it is really to act as a support, be applied firmly, and when thus applied must not interfere with the circulation. In some hands excellent results are claimed for it. One surgeon who consulted me for a severe sprain of his ankle, two days after the accident, told me he had applied the strapping as directed, but had been forced to remove it in a few hours on account of the pain produced. Probably the advocates of this method would say the strapping was wrongly applied. Surely the answer is that if in the hands of a skilled surgeon the adjustment of the supporting strapping is so difficult, the method is hardly likely to succeed in the hands of the general practitioner.

Again, the strapping must of necessity promote muscular atrophy, firstly by retarding the circulation, secondly by more or less replacing the normal muscular support, and if the muscle has no need to act, it will waste with extreme rapidity. It is this wasting, with the formation of extra-articular adhesions, which is the causal factor in the formation of a chronic sprain.

A chronic sprain could never supervene if the acute condition had been correctly treated from the outset. If the condition has become chronic it may be treated, with equal advantage, by this method of graduated contraction. The adhesions if very firm may require manipulation under an anæsthetic in order to rupture them, or may give way as the joint is gradually moved more and more, by the contractions of the muscles which normally control and move it.

The treatment of a sprained joint or muscle should begin from the first, and the earlier the case comes under treatment, the sooner it will recover.

The contractions first produced should be slight and nothing like full contraction should be attempted. The slight contractions, even in a badly strained muscle, are not painful but rather the reverse.

In dealing with a sprained joint, the muscles which move the joint are treated, and the joint moved by their action. No pain is produced, even by the joint movement, although the patient may be quite unable to move the joint himself voluntarily on account of the pain.

Treatment should be carried out daily, and for about twenty minutes; the actual amount will vary for each particular case and should never be so great as to induce fatigue.

Every case of sprain, except the most trivial, and especially all those in which the swelling obscures the outline of the joint, should be X-rayed before treatment. Some linear fractures are impossible to diagnose by any other method of examination, and although the treatment may in many cases be the same, the prognosis as to time, and the question of putting weight on the limb, may be very materially altered.

The percentage of so-called sprains, which are in reality sprains complicated by fracture, is, I think, much greater than is generally realised, and the consequences of overlooking the fracture may be disastrous.

The wrist, ankle and interphalangeal joints of the hand are those in which the mistake arises most often.

Again, a screen examination is not sufficient, but a skiagram must be taken, as often a fracture, not seen on the screen, is perfectly definite in the negative.

By the muscular contractions all the circulatory effects produced by massage are brought about, and the tone of the affected muscles is temporarily restored, giving a sense of support and comfort to the joint.

This immediate temporary improvement is really extraordinarily marked, and will, I think, be surprising to any one trying the effect of this treatment for the first time.

To describe the technique, which the writer actually uses, it will perhaps be as well to give the actual details of the treatment of a case, *e. g.* sprained ankle (right).

The leg is examined some twelve hours after the accident, X-ray examination shows no bony involvement, there is marked swelling and bruising, and the patient says he is quite unable to put the foot to the ground or move it.

The patient is placed on a couch with the right leg bare. The knee is semi-flexed over a sand bag, and under the knee is placed one electrode, a metal plate 4 by 3 in., covered with lint soaked in water. This electrode is connected to one terminal of the coil.

The other electrode, a small metal disc about the size of a five-shilling piece, is connected to the second terminal, and is held in the operator's left hand between the thumb and first finger.

The iron core of the coil is held in the operator's right hand and is fully withdrawn.

The left hand grasps the patient's muscle (beginning, say, with the peronei muscles), and presses the active electrode into firm contact with the skin. It is usual to stimulate the muscle first in the region of the motor point, and the best position can easily be found for each muscle after a little practice in using the coil. The current is passing, but there is no contraction because the core is withdrawn. This is essential.

The patient is told to relax all his muscles fully, and not to make any voluntary movement, but just to allow the foot to move as it is pulled into various positions, by the contracting muscles.

The core is then gradually inserted and withdrawn. As it is inserted the peronei contract and relax again as it is withdrawn. The foot too is dorsi-flexed and everted by the action of the muscles. The movement is quite painless, and the skin sensation practically nil.

After the peronei has been exercised for some two or three minutes, the anterior tibial group are acted on and the foot dorsi-flexed and inverted. The active electrode must not be moved from place to place, except when the core is withdrawn, or it will give rise to pain.

Again, if the patient moves or strains, the stimulation must be withdrawn, or it will be painful.

The left hand of the operator grasping the muscle, and the right hand controlling the core of the coil, the amount of contraction is under control, and can be reduced in a second.

Each group of muscles is acted on for a few minutes and the ankle will then have been moved in each direction.

No bandage is applied, and the patient is told to stand. The muscle tone will have partially and temporarily recovered, and the patient will at once notice a marked improvement.

He is encouraged to walk from the first, taking short steps, but symmetrical ones, with each leg.

Treatment is repeated next day and light massage may be ordered the same evening, especially if there is much œdema.

The patient should be walking well in four or five days, and leave off treatment in a fortnight.

Exactly the same method is to be advised in dealing with a chronic sprain.

In this case, adhesions and muscular wasting are the main factors. If the case is one of long standing, and the adhesions fail to give way after a short course of treatment, they should be broken down under an anæsthetic, and treatment begun again at once. The wasting quickly recovers, and even if a course of massage has failed to cure this condition, I have never known the treatment by graduated contraction to fail.

A marked instance of this occurred three years ago. A middle-aged lady sprained her left ankle severely. She was seen by a surgeon and X-rayed then. No sign of fracture was found. She was treated in town for two and a half months with skilled massage and movements. At the end of that time she was unable to walk for more than about 100 yards, and had considerable pain in the ankle and up the leg.

I saw her three months after the accident. In spite of the long course of massage, she had marked wasting of the anterior tibial group and peronei. I treated her by graduated contraction of the muscles of the leg, and at the end of a fortnight the pain had disappeared and she could walk a mile. At the end of a further week, *i. e.* three weeks in all, she was told to leave off the treatment.

She had some pain after walking for about a week longer, but was then completely cured. The anterior tibial group had hypertrophied to an extraordinary extent and overlapped the crest of the tibia. She reported to me six months later that she had had no further pain or weakness in the ankle.

The explanation of the success of this method in cases of this type, in which massage has failed to bring about a cure, may be that the muscle is so atrophied, that circulatory effects are of themselves insufficient to promote recovery, whilst the added chemical changes, produced by the actual contractions of the muscle fibres, are the essential factor.

Again, intra-muscular adhesions, formed by organised lymph as the result of the original muscular injury, are probably stretched and broken down, by making the muscle contract as a single unit, rather than by making the whole group contract, as by active movements against resistance.

Whatever the true explanation may be, the fact remains that so long as a muscle will contract to an induced current, it can, if wasted, be improved by this method of treatment.

The "rheumatic pains" about joints often following injury are best treated by ionisation.

Ionisation with 2 per cent. sodium salicylate solution, using as large a milli-amperage as may be borne, and for not less than forty minutes, will often relieve the pain.

This treatment should be carried out every other day unless the skin gets affected, and it is advisable to treat the neuralgic pains along the digital nerves, which may follow a sprain or fracture about the wrist joint, especially in old people, by this method.

Antiphlogistine is also of use, and is best

applied at night, when it will sometimes ease the pain very considerably.

As regards massage, light massage may be begun at once and will relieve both the pain and œdema. Massage should never cause pain, and if it does so, should at once be discontinued.

The experience gained after treating a large number of these cases of muscle and joint injury shows undoubtedly that this method of graduated contraction, by means of electrical stimulation, brings about a cure in the shortest possible time.

The ordinary acute sprain may of course be treated in most instances by massage and movements, but the recovery of muscle tone is not then so rapid, and it takes longer before the patient can resume his ordinary routine or take active exercise with the affected limb.

In some cases of chronic sprain no other method can take its place and it is essential to complete recovery. W. R. B.

TREATMENT OF DISEASES OF THE MUSCLES

DISEASES OF MUSCLES

These may be classified as follows—

Polymyositis, which includes acute polymyositis, dermato-myositis, polymyositis with erythema multiforme and urticaria.

Tuberculous Myositis, Syphilitic Myositis, Myositis due to Trichinella spiralis, Myositis due to infective organisms, Myositis ossificans, Myositis fibrosa.

Acute Polymyositis.—The acute polymyositis which occurs in association with erythema multiforme and urticaria, as a rule rapidly clears up after a short period of rest and removal of the cause of the skin affection. The administration of sodium salicylate or acetylsalicylic acid is useful. Any remaining induration is usually easily removed by massage.

The acute polymyositis or dermato-myositis which occurs as the result of some unknown toxin is commonly of long duration, sometimes running on to a fatal termination. It should be treated at first as an acute specific fever, absolute rest, preferably on a water bed, being enjoined. For the relief of pain the usual coal-tar derivative drugs should be employed. Failing relief from these, resource must be had to one of the preparations of morphia.

After the acute stage of the disease is over it is essential to prevent the permanent contraction of the muscles, and this is best accomplished by warm baths and weight extension to the limbs, followed by massage, passive and active movements.

Tuberculous Myositis is always secondary to some general tuberculous infection, and is either a direct extension from some neighbouring focus or occurs as an isolated nodule in the muscle substance. The condition calls for no special treatment.

Syphilitic Myositis occurs in its two forms, (1) Diffuse Syphilitic Myositis, (2) Gummata in Muscle. The treatment consists in the injection of salvarsan, the inunction of mercury, the administration of iodide, and, finally, massage to remove any induration which may remain.

Myositis due to Trichinella Spiralis.—The treatment of this condition resolves itself into the treatment of Trichinosis.

Myositis due to Infective Organisms.—The treatment of this condition again resolves itself into that of the general condition of which it is but a part.

Myositis Ossificans.—The slow ossification of the muscles, often starting in childhood and continuing to old age, is not amenable to any known remedy. A good deal can, however, be done for the general comfort and feeding of patients affected with this disease.

Myositis Fibrosa.—Like myositis ossificans this is a slowly progressive disease, but cases are reported in which after prolonged treatment by hot air and other baths, massage and electricity, recovery has taken place.

Muscular Dystrophies.

Myopathy.—There are various types of muscular dystrophy, and since they tend to run rather a different course it is well to consider them separately.

The following types may be recognised: (1) Simple atrophic type, amyotonia congenita (Oppenheim). (2) Pseudo-hypertrophic type. (3) Juvenile type (Erb.). (4) Facio-scapulo-humeral type (Landouzy-Dejerine). (5) Distal type. (6) Myotonia Atrophica.

Peroneal muscular atrophy should be recognised as a myelopathic and not as a myopathic disease.

Simple Atrophic Type.—This form of myopathy is characterised by smallness, lack of power and of tone in all the muscles of the body generally. The child can, owing to the loss of tone, be folded up into curious positions.

The disease is congenital, and as the child advances in years it may learn to sit up and even to stand, but full development of muscular power never takes place.

The disease as a rule advances very slowly,

but in some cases the progress is more rapid. Massage, passive and active movements and splints to prevent contraction should be used, and the child encouraged to make movements.

The pseudo-hypertrophic type generally manifests itself during the first decade of life. It is characterised by an apparent hypertrophy of certain muscles. Massage, passive movements, and moderate exercises are beneficial, and a light splint should be worn at night time to prevent contraction and deformity taking place. Injection of fibrolysin and various glandular extracts have been tried, but no benefit has resulted from their use.

The juvenile type generally manifests itself during the second decade of life, and is characterised by weakness of the muscles of the shoulder girdle. It is slowly progressive, but has in individual instances responded well to treatment and complete cures have been reported. The treatment used was massage, passive and active movements and baths.

The facio-scapulo-humeral type may show its earliest signs at birth, or in the first year of life by weakness of the facial muscles. The other signs, viz., weakness of the muscles of the shoulder girdle and pelvic girdle, may not manifest themselves till the third or fourth decade of life.

Treatment seems to have but little or no effect on the course of the disease, but the line of treatment advocated in other forms of myopathy may be adopted in this form.

The distal type is a rare form of myopathy affecting the distal muscles. It is very slowly progressive and resembles the peroneal type of muscular atrophy. The treatment consists in massage, passive movements and suitable splinting to prevent deformity and aid the patient to walk.

Myotonia Atrophica.—This form of myopathy is associated with a curious myotonic condition of the hands, somewhat similar to that seen in myotonia congenita (Thomsen's disease).

In this form of myopathy the face muscles, the sternomastoids and vasti are commonly affected. No special course of treatment is indicated.

Peroneal Muscular Atrophy.—A condition in which atrophy begins in the peroneal muscles and those below the knee and affects also the small muscles of the hand. It occurs in families, affecting male and female alike.

Patients suffering with this complaint are able to continue work for many years. The treatment advocated in the distal type of myopathy is suitable for this class of case. F. E. B.

Note.—For Myasthenia gravis, see "Diseases of the Nervous System."

For Fibrositis, see article on "Neuralgia."

TREATMENT OF DISEASES OF THE VASOMOTOR SYSTEM AND TROPHIC DISORDERS

I. Raynaud's Disease

The disease consists in a periodic constriction of certain arterial fields, external as well as internal, resulting in varying grades of ischæmia which in its effects on the tissue concerned may cause either a temporary stasis or even a total gangrene. It is necessary to bear in mind its arterial causation so that treatment may be directed into the right channels. A preliminary Wassermann reaction is essential, and a history of malaria should be inquired for.

General Treatment.—The arteries are more liable to be irritated by toxins which stimulate their muscular coats in depressed conditions of health, therefore the patient must abide strictly by ordinary rules of health so that his body may have the chance of righting itself naturally if this be possible. Digestion must be inquired into carefully and all possible irritants eliminated, especially excess of meat foods and highly seasoned dishes. The patient must have a light nourishing diet at reasonable intervals. The bowels must be kept loose and the intestinal tract freed from an undue amount of bacterial fermentation. For this an occasional mercurial purge has no equal. A very small quantity of a pure alcohol such as a tablespoonful of whisky or a glass of white wine may be allowed with the two principal meals. All conditions which may assist or aggravate the production of arteriosclerosis must be rigidly eliminated; such are: alcohol except in the strictest moderation at meals, tobacco, excessive mental work and worry. A high blood pressure must if possible be lowered. Inasmuch as cold tends to cause arterial constriction of the peripheral arteries the patient must be protected from it and if possible be made to reside in a warmer climate during the winter. Finally a yearly visit to one of the spas such as Carlsbad with mild aperient waters will tend to assist in the elimination of waste or harmful metabolic products.

Drug Treatment.—There is no drug which can be depended on to relax the spasm when once it has occurred or to prevent its onset, but nevertheless the vaso-dilators often produce

a marked change for the better and should undoubtedly be given a careful and prolonged trial. Two are to be commended, the nitrites and thyreoid gland substance. The best of the former are either erythrol tetra-nitrate (initial dose $\frac{1}{4}$ gr.) or mannitol hexa-nitrate (initial dose 1 gr.). Of thyreoid, the solid, dried substance compressed into tablets or tabloids (initial dose $\frac{1}{10}$ gr.) gives all that can be desired. With these substances it is necessary to begin with the smallest dose and gradually to work up to as large a dose as the patient can stand so as to accustom the body to its effects. The nitrites are practically harmless thus used, but the use of thyreoid extract in old persons must be checked by constant observations on the pulse-rate and condition of the circulation, any tendency to faintness or lassitude being a sign for caution. The hippurates of sodium and ammonium (initial dose 5 gr.) have been warmly recommended by Oliver.

Local Treatment.—(*a*) During the attack the indications are to relieve the pain, to restore the circulation and to treat the gangrene. For the pain morphia may be required, but in view of the recurrent nature of the affection milder analgesics should be tried such as: chloretone 8 per cent. in olive oil or "anæsthesine" 2 per cent. in almond oil. For the restoration of the circulation Cushing recommends the hyperæmia which follows the use of Esmarch's bandage when applied to the affected limb for half an hour; instead of a bandage an ordinary tourniquet may be used. Gentle massage will assist in the restoration of mild grades of ischæmia. The gangrene must be treated according to the rules of surgery.

(*b*) In the interval of an attack all methods which tend to increase the circulation in the part are useful. Such are gentle friction and massage (skin friction and muscle kneading); alternate hot and cold douches; radiant heat (daily applications for half an hour to such a temperature as will give a good vaso-dilator reaction); and finally the battery applied as a constant current; Barlow recommends the limb to be immersed in a saline bath of tepid water, one pole of the battery being the basin, the other placed in contact with the upper part of the limb. The current should be frequently broken and as high a current as possible used.

II. Intermittent Claudication

The arteries in this condition are the source of the symptoms; both clinically and after death they can be found markedly arteriosclerotic and the pulsation in one or more of the arteries to the part are found to show diminished pulsation when the condition becomes acute. The treatment must be directed, therefore, first to removing those factors which may be the source of the arteriosclerosis (*q.v.*). It may be permitted to mention that Erb has recently determined that this disease attacks excessive smokers more frequently than others and that the removal of this agent causes a marked amelioration in the symptoms. There are no doubt other toxins which cause intermittent claudication, for it occurs in women who have never smoked, but in view of this fact persons so afflicted should avoid tobacco entirely.

Prolonged treatment with large doses of potassium iodide is probably the best drug to use.

As regards local treatment, the limb should only be used short of producing unpleasant symptoms. Massage, radiant heat and the constant electric current should be used systematically in turn so as to assist the normal circulation of the limb and help to restore the natural elasticity of the arteries.

III. Erythromelalgia

The part should be rested in that position in which least pain occurs for such a time as is required to restore the vessels to their normal condition. Gentle massage if it can be comfortably borne is perhaps the best way to assist the restoration, but all forms of local treatment such as wet packs, radiant heat and electrical treatment tend to assist recovery.

IV. Angioneurotic Œdema

This is a condition in which occasional or periodic œdematous swellings appear on the surface of the body, tongue or larynx accompanied at times by severe gastro-intestinal symptoms such as pain and vomiting.

General Treatment.—An endeavour should be made to improve the general health of the patient by correcting any defections from strict hygienic rules. It is questionable whether diet is a prominent factor in its production, but on the assumption that it may be an arterial affection the amount of meat taken should be reduced to a minimum. Coffee and tea should only be taken sparingly. The bowels especially should be carefully regulated, preferably by means of salines, and any excess of bacterial fermentation should be corrected by antiseptics such as small doses of grey powder.

Of *Drugs* none are specific against the affection, but two are useful and should be given serious trial. Calcium lactate, which is recommended by Wright, may be given in 15-gr. doses thrice daily; in some cases this has produced remarkable benefit.

The other drug is nitroglycerine or one of its allies such as erythrol tetra-nitrate (initial dose $\frac{1}{4}$ gr.) or mannitol hexa-nitrate (initial

dose 1 gr.) thrice daily, which should be gradually increased until the unpleasant effects of the drug, flushing, throbbing or slight transient faintness, are felt. After that the patient should interrupt the treatment for a few days every fortnight. In children and old persons the effects of the higher doses should be carefully watched.

During an attack, if gastro-intestinal, it is well to withhold a hypodermic injection of morphia unless suffering is extreme. A strong carminative such as a drachm of aromatic spirits of ammonia with two or three drops of oleum carui in an ounce of hot water is the best routine draught. A hot-water bag to the abdomen may relieve some of the intensity of the pain.

Attacks which affect the eyelids or hands do not require any more treatment than protection of the area from cold and injury.

Œdema of the larynx may bring on serious asphyxia which can only be treated by tracheotomy or intubation, and the necessary instruments for both should be at hand in case of recurrent attacks. Œdema of the tongue, though not so dangerous to life, is sufficiently serious to require urgent interference, which is best done by making several needle punctures into the œdematous organ so as to allow the fluid to drain away.

V. Scleroderma

This affection has as its anatomical basis a sclerosis of the small arterioles of the skin together with a general arterio-sclerosis. The underlying agent, whether infective or toxic, which produces it is unknown, and it is the first element in treatment to eliminate all possible sources of absorption. The meat in the diet should be reduced to a minimum and the bowels kept thoroughly free. In certain cases thyreoid therapy has produced good results, though only occasionally may a cure be expected. Extremely small doses should first be given, $\frac{1}{10}$ gr. twice daily, to be increased gradually to 5 gr. twice daily, and under this treatment the pulse-rate should not be allowed to rise above 100 at rest. A thorough trial of X-rays should be given, and all methods such as massage and hydrotherapy designed to preserve the suppleness of the skin are useful.

VI. Facial Hemiatrophy

Too little is known of the cause of this condition to allow more than the mention of palliative treatment. On the evidence from one case the atrophy has been assumed to be the result of an interstitial neuritis of the trigeminal nerve, and it is legitimate to suppose that other cases may be due to an inflammatory or at least a toxæmic cause. It is therefore desirable to overhaul the patient in order to find out if there be an absorption of such material from some focus. The teeth, nasal sinuses, tonsils and alimentary tract are the most likely; moreover, the possibility of a syphilitic or tuberculous infection should not be lost sight of. Little can be done when once the atrophy has set in to remedy the condition, but injections of paraffin have been used with success to restore in some measure the fulness of the tissues. Massage tends to keep the circulation efficient and to delay muscular atrophy.

A. G. G.

TREATMENT OF DISEASES OF THE SKIN

THE DIETETICS OF SKIN DISEASE

This is a difficult subject, of considerable importance, about which much has been said and written, but about which little is known. It is, of course, obvious that substances ingested must have some effect upon the skin, but that effect is in most cases vague and seldom can be ascertained to follow any definite rule. The idiosyncrasies of individual patients are so extremely marked that it is impossible to make any real generalisation about it. Those patients who suffer from a severe degree of alimentary toxæmia which is manifested in various ways, seem, for the most part, to be immune from any striking manifestation on the skin. The worst that can be said, as a rule, of that organ is that their complexion is affected. On the other hand, it is well known that certain foods always cause in certain people an attack of urticaria which may be of any degree of severity. Here the idiosyncrasy of the patient is so conspicuous that it is the determining factor. On the other hand, foods which are slightly decomposed are much more likely than wholesome articles to give rise to cutaneous symptoms, and urticaria is a common accompaniment of ptomaine poisoning. The urticaria, which is associated in some individuals with the ingestion of foods which are innocuous to most people, is a form of anaphylaxis to certain proteins.

Nevertheless, although so little is really known of the influence of food on the skin from time immemorial, physicians have not hesitated to prescribe the most exact and rigid dietary rules for their patients. The favourite plan is a

severe limitation of fish and meat, and occasionally absolute vegetarianism is inculcated. There is little scientific evidence for a very strict dietary in cutaneous disease, although certain articles of food are undoubtedly injurious to certain patients. We shall only be in a position to give exact dietetic directions to patients suffering from skin disease when we know far more than we do now of the detailed chemistry of foods, and the exact transformations which they undergo in the processes of digestion and assimilation. Biochemistry is still in its infancy, and until it is much further advanced it will be impossible to have an accurate knowledge of the real effect of different foods upon the skin. All that can be definitely affirmed at present is that the amount of food should be proportioned to the patient's needs. Over feeding is well known to be frequently associated with an outbreak of eczema, and eczema is also equally common in the half-starved casual labourer. Either of these classes is benefited by receiving a diet appropriate to his physiological necessities.

An acute inflammatory disease of the skin is often, in the well-nourished, benefited by a few days' initial starvation or semi-starvation, while occasionally it happens that a patient is found who, although in good worldly circumstances, has been so strictly dieted and reduced to such a pitch that he improves greatly by being fed up. All of which means that the diet in skin disease must be regulated according to common sense, and not according to any superstition.

There is, however, one important element in the skin which can undoubtedly be definitely affected by drugs if not by foods, and that is the vascular system. Agents which are prone to increase the capillary blood pressure, and thereby cause hyperæmia of the skin, are undoubtedly detrimental, and should be avoided by dermatological patients. The chief of these substances is alcohol. In susceptible subjects abuse of alcohol alone is undoubtedly adequate to set up definite dermatoses, especially acne rosacea, and its use, even in moderation, is often sufficient to prevent a chronic skin affection from yielding to treatment. There are, however, patients whom nothing will induce to surrender their drink, and for these it is now the fashion to prescribe whisky. There is something to be said for this, because it is usually taken well diluted, but if the patient is inclined to take it in a concentrated solution it should be vetoed altogether, and a minimum quantity of light claret alone allowed. Other articles of diet which are inclined to produce flushing of the face, and which are consequently injurious to sufferers from acne rosacea and eczema, are hot and highly spiced foods. There is a widely spread, and possibly well-founded, prejudice against twice-cooked meat. But this is an example also of a restriction often advised without any real scientific evidence.

Among children who suffer, as so many do, from that distressing eruption known as lichen urticatus, strophulus, erythema infantum, or, more popularly, gum or teething rash, there is no doubt that an excess of carbohydrates in the food is often highly injurious, although here, again, the way in which they act is quite obscure, and our only justification for their restriction is purely empirical. Simple directions, which are often sufficient to give the mother, are: "No bananas, no potatoes, no sweets." Moreover, after the age of a year to fifteen months it is wise to give an infant a little meat once a day.

Many physicians have attempted to treat that mysterious disease psoriasis on dietetic principles, and some have strongly advocated vegetarianism; all that we can say is that the results are not sufficiently striking tojustify this régime as a routine prescription.

H. D.

INTERNAL MEDICATION IN DISEASES OF THE SKIN

The old idea that all skin diseases are the outward expression of some abnormal condition of the blood appears to me to be so prevalent still that I think it necessary to state at the outset that many diseases of the skin require no internal medication at all.

It is, for instance, not uncommon to hear the statement made that children who catch ringworm do so because they are in an enfeebled state of health, a statement which is not confirmed by unprejudiced observation, and I have also been told frequently that aperients are required in the treatment of scabies.

Now although it is conceivable that at some future date forms of internal treatment may be discovered which are specifically curative of ringworm or scabies, it is quite certain that at the present moment no internal remedy is known that has the slightest curative action on either of these diseases.

There are, however, some substantive skin diseases and abnormal conditions of the skin in which internal medication is of value, and these may be divided into two classes, namely, those in which certain general forms of internal treatment are advisable owing to their being frequently associated with errors in the general condition, and those in which a specific treatment is known acting directly on the disease itself. In this article only the first class will be referred to, since the second is dealt with in connection with the individual diseases.

1. There is a class of skin disease in which it would seem that the irritability of the skin generally is much increased and in which after

the removal of the prime cause of local irritation the skin continues to react by the formation of scattered acutely inflammatory lesions to stimuli which in normal health would be negligible.

In such cases there may be a real error of metabolism at work or the condition may have been produced by repeated or long-continued irritation of the skin by a local cause.

Such cases are generally classed as "Gouty eczema" without any serious attempts being made towards unravelling their often complicated etiology.

They may sometimes be treated with benefit by means of a series of remedies which have one action in common, namely, that of acting as a depressant. Among these remedies we may mention antimony, in doses of 10 to 15 min. of the wine, saline aperients and many mineral waters such as the strong sulphur waters of Harrogate and Luchon.

In most cases it is probably better to use those salines such as magnesium or sodium sulphate which are either not absorbed at all or at any rate in very small quantities.

When attempting to subdue irritability by this method it is important to keep the patient on a low diet for a short period, and the best form appears to be a diet of milk (2½ pints a day) with a very limited amount of solid food such as twelve thin captain's biscuits a day.

It is to be understood that these measures are not advised with the idea that such treatment is good for the patient if persisted with, but merely as a temporary expedient. They must not be used on the weakly or aged patient, and the starvation diet should not be adhered to for more than a fortnight.

2. A second class of case exists in which the eruption, whatever its nature, is apt to be complicated by what may perhaps be best described as an urticarial basis.

These cases are generally more or less eczematous in type, but the tendency to œdema is much more marked than usual. The patients have not infrequently a somewhat diffluent subcutaneous tissue so that the skin feels very soft, and is easily picked up into folds. They often suffer from chilblains in moderately cool weather and have a general tendency to acrocyanosis, and the bites and stings of insects usually call forth an exaggerated reaction.

In such patients a careful inquiry should be made into the amount of common salt which is habitually ingested. Physiologists have found that the skin is the organ by which excess of sodium chloride is taken up and retained, and there is no doubt that an excess of this salt may cause œdema. These patients should therefore be instructed to avoid very salt articles of diet and to take no salt in addition to that put in with the cooking.

Three drugs are credited with the power of exerting some control over this tendency to sudden œdema, namely, quinine, ichthyol and the salts of calcium.

Quinine is probably the most certain in its action, but it should be given only for a short time as it is necessary to use large doses to obtain the desired effect. It is my custom when using this drug to prescribe 5-gr. doses with a drachm of dilute hydrobromic acid in a wineglassful of water three times a day after food. Such doses should not be continued for more than a fortnight at most.

Ichthyol may be given in capsules or in keratin-coated pills in doses of from 5 to 15 min. three times a day. It appears to be quite innocuous, but I have not very often found it of service.

Salts of calcium such as the lactate or chloride are given with the idea that they thicken the liquid part of the blood and so inhibit its diffusion through the capillary wall, but it should be remembered that calcium salts are also cardiac stimulants, and some of the benefit may be due to improvement in the circulation.

Calcium lactate may be given in large doses (2 dr.) twice a week or in small doses (10 gr.) three times a day. In either case the treatment should be intermittent; for instance, a fortnight's taking of the drug followed by a week's abstinence. It is nearly tasteless and is soluble if freshly prepared. Calcium chloride may be given in 10-gr. doses three times a day, but it is very nauseous and does not appear to be so well absorbed.

3. The eruptions generally grouped as "seborrhœic" which are associated in most cases with excessive secretion of the sweat and sebaceous glands may be attacked by an attempt to diminish these secretions.

The drugs which appear to have an action in this direction are belladonna, menthol and sulphuric acid.

Belladonna is the most powerful, but if given in sufficient doses is apt to produce other effects uncomfortable to the patient, such as dryness of the throat and perhaps a rash. I therefore seldom use it alone.

Menthol has three actions which are often desired together, namely, it is an excellent carminative, it is a moderately efficient antiseptic, and it has a distinct anhidrotic and antiseborrhœic action. It may be given in capsules in doses of 1 to 2 gr. three times a day after meals and may be continued for long periods.

Sulphuric acid, an old-fashioned drug, seems to me to deserve its old reputation for diminishing cutaneous secretions. It may be

given in doses of 10–20 min., well diluted, and if constipation is caused 15 gr. of sodium sulphate may be given with it. It is also credited with the effect of fixing and rendering inert any excess of indol and skatol, converting them into indoxyl and skatoxyl sulphate.

4. There are also certain conditions of whose etiology and pathology we have no knowledge, but which are suspected of being due to alimentary toxæmia and autogenetic intoxication.

To combat the supposed intoxication we may attempt to increase elimination by the bowels and kidneys and to diminish the production of poison by means of internal antiseptics.

To increase elimination there is probably no drug of so high a value as water, and I have on more than one occasion seen persistent skin troubles of unknown origin clear up on the addition of three or four pints of plain water to the patient's diet. I am still doubtful how far the benefit derived at most of the watering spas is due to the large amounts of water drunk there, but it seems to be quite certain that much of the benefit is due to this.

The late Dr. Radcliffe-Crocker recommended short courses of turpentine internally as a diuretic with the view of increasing elimination from the kidney, and I am quite confident that I have seen marked benefit result from the use of this drug. It should be given in 10–15 min. doses three times a day, and the urine must be carefully watched for signs of renal irritation.

To increase elimination by the bowel either blue pill may be used in doses of 2 gr. twice a week or small doses of calomel ($\frac{1}{12}$ gr.) may be given three times a day. The latter may possibly act partly as an intestinal antiseptic in these small doses. Daily use of salines such as magnesium or sodium sulphate may also be tried.

Of the drugs which act as internal antiseptics without aperient action those chiefly used are salol and salicin, β-naphthol, and creosote or guaiacol carbonate. To all of these I have given a fair trial, and although in some cases I have thought that benefit has been derived I have found them on the whole disappointing. This is scarcely surprising since we do not really know first whether there is any relationship between the skin condition and the alimentary tract, nor, secondly, that the supposed antiseptic has any such action in a marked degree.

As regards the sour-milk treatment, which had such a vogue a few years ago, I can only say that beyond a slight aperient action in a few cases I have seen no effect.

Lastly, there are two drugs, sulphur and arsenic, whose reputation with the lay public and some medical men is such that it is desirable to make some special mention of them.

Sulphur has perhaps a greater reputation as a local rather than an internal remedy, but the fame of the sulphur springs shows that the internal use of it is still popular.

After a considerable experience of the internal use of sulphur as the simple element I have to come to the conclusion that it is an extremely valuable aperient for habitual use, but have been quite unable to decide whether it has any further action of importance. I can, however, say that I have never seen any harm attributable to its internal use.

Arsenic is of course a most potent drug with a special action on the superficial parts of the skin. It has the reputation of producing a fine type of clear complexion, but this I believe to be quite unwarranted. I have seen many patients who have taken it over long periods, some of whom showed definite arsenical changes in the skin, and in none has there been any particular clearness of the complexion.

The drug seems to have a stimulating action on the papillary body and epidermis, and may occasionally act beneficially in rousing up extremely sluggish conditions such as chronic scaly affections of the palms, soles and lower extremities. Except in those cases such as lichen planus, psoriasis, etc., where a more or less specific curative is noticeable, it should not be used in any severely inflammatory affection, and even in those diseases already mentioned it is somewhat risky to give it in the acute stages.

In my opinion it is better not to give arsenic internally except in those diseases in which its existence is known to have a specific curative action unless it is used only in small doses as a general tonic in anæmia and debility.

A. W.

GENERAL THERAPEUTICS OF LOTIONS AND OINTMENTS

All fatty and greasy medicaments for external application are termed ointments. They have been used for the comfort and healing of the skin since the earliest times. They are frequently mentioned in the Bible and also in the Classical writers. Some of the references suggest that they were employed chiefly for cosmetic purposes, and that the modern "skin-food" had its ancient prototypes. Ointments are perhaps not so much used at the present time as they were before the discovery of the principles of antisepsis, as there is a tendency to regard them as dirty and messy, and also as somewhat inclined to encourage microbic life. There is no doubt, however, that they are still extremely important in dermatology, and we should often be extremely embarrassed if deprived of their assistance. Ointments are used

for the following purposes: (1) As a protective covering to inflamed and, therefore, hypersensitive surfaces. (2) To prevent the evaporation of fluid and the consequent formation of crusts when the skin is broken, with the formation of an ulcer or a raw surface. (3) To soak up discharges. (4) As media for the application of drugs which may be antiseptic or may have some more obscure action on the growth of the cells of the epidermis. In many cases ointments are intended to fulfil two or more of these purposes simultaneously. The nature of the fatty substance or base employed must necessarily differ greatly according to the duty the ointment is intended to fulfil. The ointments of antiquity, it seems, were really oils, those of a less distant but pre-antiseptic era were usually made up with lard, an excipient which, when quite fresh, is excellent, but which possesses the grave disadvantage of quickly becoming rancid and offensive. At the present time it is seldom used pure, but has added to it 2 or 3 per cent. of tincture of benzoin. This prevents it from being rancid, but causes it to become slightly irritating and, therefore, unsuitable for very sensitive surfaces, such as the conjunctiva. The only other animal fat frequently employed at the present day is lanoline, or wool fat. This is seldom employed pure, however, because it is too stiff for incorporation to make a pleasant preparation; it is usually added in rather small proportions to ointments, on account of its property of absorbing considerable quantities of water. This property is possessed in a still higher degree by some of its derivatives, such as eucerin. The employment of the higher members of the hydrocarbons as ointment bases is comparatively modern, but is now common. They were introduced into dermatology about 1877 by Unna. They are known as the hard and soft paraffins. These bodies are extremely convenient because they can be made up by suitable mixture to form a base of any required consistency; they are quite innocuous, even to the most tender surface, most drugs can be easily incorporated with them, and chemically they are very inert, so that they have no tendency to decompose or become rancid. The commercial "vaseline" is merely another term for soft paraffin, and white vaseline is soft paraffin which has been filtered through animal charcoal. The only disadvantage of the paraffin bases is that their power of penetrating the skin is not equal to that of the animal fats. Ointments should be made up with these bases, except when deep penetration is desired.

Modified ointments are pastes and creams. Pastes only differ from ointments in being to a certain extent porous, and, therefore, they soak up a certain amount of discharge and permit evaporation from the surface. These qualities are usually obtained by the addition of a quantity of starch. Pastes are also sometimes made up with other constituents, such as tragacanth or gum acacia.

Creams are of several kinds. In the first place there are oily excipients, with which various drugs may be incorporated, of these the chief is the well-known carron oil or liniment oleo-calcaire of French writers, and, in the second place, there are creams of the class of skin food or massage paste, and, again, there are a number of preparations all of which may be termed cold-creams. All the modern "skin-foods," or massage pastes, are made up with a basis of casein or of a vegetable jelly, such as quince mucilage, Irish moss, or tragacanth.

Again, "cold-creams," which form another class, owe their cooling properties to the evaporation of rose water imprisoned among the fat globules. There are countless formulæ, the following is a simple one—

Borax gr. xx
Parolein ℥ ii
White Wax ℥ ii
Rose Water ℥ ii.

Lotions may be divided into five groups: (1) Cooling lotions, (2) emollient lotions, (3) antiseptic lotions, (4) protective lotions, (5) astringent and stimulating lotions.

Cooling lotions owe their properties to the inclusion of a fair proportion of spirit. They are most used in cases of injury to joints and tendons, where there is considerable local inflammation with the outpouring of fluid.

Emollient lotions are conspicuous among the complexion lotions sold by the chemist and beauty specialist. Although differing very widely in appearance and perfume, they all owe their emollient powers to the presence of glycerine. This substance, when diluted down to about 1 or 2 per cent., prevents the epidermis from drying and, therefore, keeps it soft and hinders desquamation.

Antiseptic lotions are, perhaps, those most commonly used in medicine. They include all the lotions made with mercuric salts and from the coal tar derivatives, not to speak of many others familiar to every medical man. It is unnecessary to go into these in detail, but it is right to warn the practitioner against using strong solutions. Weak solutions are quite adequate to clean the surface, and strong solutions, while unable to penetrate deeper, may do much harm to the tissues. Some of the so-called "beautifiers" belong to this class, they consist of solutions of perchloride of mercury, and act by curing mild forms of acne.

In protective lotions some form of powder is suspended which is deposited upon the skin as

the lotion dries. The powder is usually suspended in a lotion of the emollient type. The substance which forms the basis of most protective lotions is a compound of zinc, either zinc oxide or calamine. Lead acetate is also often employed.

Stimulating and astringent lotions are used to promote healing of ulcerated and raw surfaces. They contain small percentages of metallic salts, usually zinc or silver. Lately colloidal metallic solutions have been introduced and are meeting with some favour. H. D.

THE CARE OF THE COMPLEXION

This is a subject upon which medical men are often consulted, but to which they pay, as a rule, little attention. Although it is an undoubted truth that a silk purse cannot be made out of a sow's ear, nevertheless a good deal can certainly be done in this direction without resorting to the use of cosmetics, which may hide but do not remedy defects.

The complexion may be affected by many factors. In the first place a most important point is the maintenance of the general health in its fullest vigour. At one time novelists were accustomed to invest their consumptive heroines with a cutaneous covering of delicate tint and fine texture, but even they only got the full benefit of these advantages during the periods of intermission of the disease. In ordinary experience it may be affirmed that the complexion of the consumptive is anything but attractive. At the same time it must be admitted that occasionally one sees very delicate and beautiful colouring in persons who are predisposed to phthisis, but who have not yet developed it. In chlorosis also the patients sometimes exhibit an artistic pink and white cheek, although usually there is an admixture of yellow which quite spoils the effect.

Constipation is perhaps the condition most commonly associated with a dull and muddy complexion, and the improvement to be hoped for in this direction is a powerful argument in favour of a proper regulation of the bowels, a point which the female sex is prone to disregard. For this reason I have known great good result from a course of skilled abdominal massage. Spots on the face, indicative of a lowered degree of health, are often associated with some septic condition of the mouth or pharynx, and I have noticed a little girl's complexion clear up in a marvellous way after the removal of septic tonsils, and great improvement in an adult as the result of treatment of pyorrhœa. The quality of atmospheric environment exercises an influence apart from its effect upon the health. The best climate is one which is cool and not too dry. Hence the high average of the complexions of the inhabitants of these islands, especially of Ireland. The worst is a hot, dry atmosphere, such as that of India or the artificially warmed houses of America. Open-air exercise, of course, is beneficial, but exposure to the elements in all weathers coarsens the skin. The effects of sun and wind may be observed in the freckled faces of the peasant women who work in the fields.

Local Methods of Treating the Face.—Apart from the treatment of the more obvious dermatoses of the face, such as acne and eczema, there are several points to which attention may be directed.

1. *The Proper Cleansing of the Skin.*—The face should always be washed before going to bed. After the day's exposure there must be a certain amount of extraneous matter adherent to the skin; the removal of this gives the skin a proper opportunity to recover during the hours of rest. Some women can use soap for their faces with impunity, others, however, are too sensitive, and these should employ plain water softened with oatmeal. Perhaps more convenient, and undoubtedly more expensive, are the scented starch sachets purveyed by fashionable chemists. Some never use water for the face at all, but always oily preparations. Simple liquid vaseline or almond oil are as good as any others more elaborate, and the shiny appearance which may remain after their application may be removed readily by the application of ordinary toilet powder. It has long been a superstition that the use of greasy preparations, especially of animal origin, encourages the growth of hair on the face, but I doubt if there is any real foundation for this belief. I have known slight but long-persistent eczema of the face yield very quickly after this method of cleansing has been adopted.

It is a good habit to steam the face every night, especially after a fatiguing day; this is not only refreshing, but, by exciting glandular secretion, helps in washing out foreign matter from the follicles.

2. *Face-massage.*—This is one of the most useful methods of preserving the complexion, and it has the additional advantage of being very pleasant and refreshing to the patient. It can be given either by means of a mechanical vibrator actuated by electricity or by hand, or, preferably, both methods should be combined.

The chief movements made use of in facial massage with the hand are—

(a) *Plucking.*—In this the skin is gripped between the forefinger and thumb, pinched firmly enough to cause a slightly painful sensation, pulled and suddenly released.

(b) *Stroking* gently but firmly in the direction of the venous flow.

(c) *Hacking.*—This is done by striking the

cheeks with the ulnar border of the hand and the backs of the three outer fingers, which must be held with the joints loose.

Massage is useful for increasing the circulation, and therefore encouraging the complexion to become brighter, and it also stimulates the facial muscles and causes them to contract reflexly. The result is that they are all regularly exercised and thus become firmer. Largely for this reason massage is valuable in the prevention or, at any rate, in the retardation of wrinkles, and to a lesser extent in their removal. I have seen great improvement take place in the complexion of a patient approaching middle age after a course of skilled massage of the face, especially if it were the first time the patient had been treated in this way. A word of warning: patients suffering from rosacea should never have face massage.

It is usual for the masseuse to employ in her work a lubricant for her fingers, and of these lubricant preparations there have been devised a great variety. Among them are included the great host of skin foods and vanishing creams which have often usurped the credit which is really due to the massage. The essentials of these preparations are that they should be both pleasant and harmless. As they are used constantly and repeatedly they must be absolutely devoid of all irritating properties. One of the simplest and most satisfactory formulæ is as follows—

Borax gr. xx
Rose Water ʒ ii
White Wax ʒ ii
Parolein ʒ ii.

Many are made with stearic acid and sodium carbonate, and in these it is essential that the stearic acid should be in excess. The following makes a good formula, especially for a skin which is not prone to become dry.

Stearic Acid, 12 parts
Sodium Carbonate, 2 parts
Glycerin, 1 part
Water, 85 parts.
Perfume q.s.

A good cream can be made by precipitating the casein from milk and washing it. This, however, does not keep well.

Another good and simple cream can be made by carefully melting together one part of lanoline and one part of soft paraffin and adding one part of glycerin when the mixture is nearly cool. H. D.

ECZEMA

It is necessary in the first place to have a clear idea of what is meant by the term eczema. For the purposes of this article eczema will be defined as an inflammatory disease of the skin, non-microbic in origin, characterised by a certain amount of exudation into the skin which usually causes the formation of vesicles and sometimes of a discharge of serum. In almost all cases of eczema local irritation plays some part in the etiology, but some individuals are undoubtedly predisposed to the disease, for in them a degree of local irritation which to most people is absolutely innocuous gives rise to a violent attack. The importance of local irritation not only in determining but also in keeping up an attack of eczema can scarcely be overrated, and in every case the keynote of treatment should be the protection of the part of the surface affected. The treatment of predisposing factors, *i.e.* the internal or constitutional treatment of eczema, is much more difficult and less satisfactory, for in most cases we do not know what those predisposing causes really are. Gout is very commonly ascribed as a cause of eczema, and it is true that some gouty patients have eczema; but nobody yet knows what gout is, and moreover many patients are told that their eczema is due to gout although they have never suffered from any other manifestation of the disease. Similarly, eczema is often attributed to an "acidity of the blood," or even to conditions still more vaguely defined than that, and which are quite incapable of accurate description and consequently of scientific treatment. In fact, the only internal treatment of eczema which is really reasonable is the avoidance of excess of every kind and a proper regulation of the bowels.

In this article attention will be given principally to local treatment. For convenience of description the treatment of eczema may be divided into several sections. The treatment of acute eczema may be separated from that of chronic eczema, and again there are also peculiarities according as the disease affects different situations which require separate attention.

Acute Erythematous Eczema for the most part affects the face and genital organs. It gives rise to all the classical signs of inflammation locally but there is not much general constitutional disturbance. Particularly conspicuous is the great swelling owing to the loose characters of the tissues in these parts. In the initial stages the patient should be confined to bed or if that be impossible should at least be forbidden to go into the open air. Locally one must apply a cooling preparation. The writer always uses the cream made up according to the following formula—

Zinc Oxide ʒ i
Lanoline ʒ i
$\left.\begin{array}{l}\text{Lime Water}\\ \text{Olive Oil}\end{array}\right\}$ āā ad ℥ i
Perfume according to taste.

Owing to the large quantity of water which this preparation contains it has marked cooling properties. No acutely inflamed surface must be washed with water, and therefore when it is desired to apply fresh cream the previous dressing is carefully removed by means of liquid paraffin on cotton-wool. The cream should be renewed at least twice daily. As the inflammation subsides and exudation ceases the astringent properties of the cream are improved by the addition of half a drachm of ichthyol to every ounce. This modification often has a most marked effect upon cases which are hanging fire a little.

Eczema of the face in infants differs somewhat from that met with in adults in that it is rather of the vesicular type while in adults it is erythematous. For infantile eczema the best preparation is a zinc paste similar to the well-known Lassar's paste but without any salicylic acid. The following is the formula—

Zinc Oxide ʒ ii
Starch ʒ ii
Vaseline ʒ iv.

This paste should always in children be applied spread on a mask of butter muslin. It is also an essential of treatment in infants to prevent them from scratching. This is best done by enclosing their arms in cardboard splints.

If the surface weeps at all the dressing must be changed at least once if not twice in the twenty-four hours. The surface must be cleansed with liquid paraffin, not with water, but there is no need to use any force at all to get off all the paste, which at times adheres rather tightly. If there is no discharge, if the child seems comfortable and can be fed without dirtying the mask round the mouth, there is no reason why it should not be left undisturbed for forty-eight hours or even more at a time. Eczema of the face in infants varies very much in its response to treatment in different cases. Sometimes it can be cured quite easily, sometimes it is very resistant to treatment. Occasionally in these obstinate cases it is found beneficial to paint the surface two or three times a week with a 2 per cent. solution of nitrate of silver. In any case it is very rare to see eczema of the face persist after the age of two years.

Perhaps the commonest form of eczema which occurs in adults is *trade* or *occupational eczema*, which may be either of an acute or chronic type. Here there is definite local irritant at work and effective treatment is almost impossible until the patient is removed from its action. The parts affected by this form of eczema are always and principally the hands, and the eruption usually extends a varying distance up the forearms. In particularly sensitive subjects a widespread attack may occur. In these cases as in others the simplest applications are the best, and chief reliance should be placed on the zinc paste and cream, the formulæ for which have been given above, in combination with liquid paraffin as a cleansing material in place of water. As a rule these measures will effect a speedy cure, but it sometimes happens that patches, more or less discrete, remain after the acute inflammation has subsided, usually upon the hands, forearms and wrists. These patches sometimes persist for long periods of time and often require some little management in order to induce them to disappear. The condition of the skin in these cases is best described as one of sluggish metabolism in which the cellular processes, whereby the epidermis is continually being shed from the surface and renewed from below, are carried out in an irregular manner. In order to cause a reversion to a normal state it is often advisable cautiously to stimulate the skin. This may be done in several different ways. (1) Some reducing agent may be added to the zinc paste. The best of these is lenigallol which may be added in the proportion of half a drachm to an ounce of paste. Or (2) tar preparations may be tried; those most frequently used are the Liquor Carbonis Detergens and the Liquor Picis Carbonis. A good formula is as follows—

Liquor Picis Carbonis ʒ i
Hydrarg. Ammon. gr. x
Vaseline ad ℥ i.

Tar preparations must never be used when the skin is acutely inflamed. (3) In very long standing cases of chronic eczema in which a few vesicles persist in appearing after the greater part of the disease is cured it is sometimes useful to paint them with liquor iodi once or twice a week. (4) Another remedy for chronic eczema, which, however, must be used very cautiously, is a *very weak* chrysarobin ointment, ten grains to the ounce. (5) Still another method of applying local stimulation to a chronic patch of eczema is to paint it occasionally with a solution of silver nitrate in Spiritus Ætheris Nitrosi (5–20 gr. to the ounce), immediately afterwards covering it up with lint spread with zinc paste and leaving it *in situ* for twenty-four or forty-eight hours.

(6) Perhaps the most useful method of stimulating patches of eczema is by small doses of X-rays, one-third to half a pastille dose for a series of three doses, with a rest of at least a week after each dose. In almost every instance the infiltration disappears and the patch clears up, and, what is most appreciated by the patient, the irritation stops as if by magic.

Eczema complicated by Sepsis.—It frequently happens, especially in neglected cases, that eczema is complicated by pyogenic infections.

In this case the condition of the patient is much aggravated. The complication is to be recognised either by the purulent nature of the discharge and by the thick and yellow character of the crusts which are formed or by the presence of boils and furuncles. The first step in treatment must always be to clear up the sepsis. This is to be done on the ordinary lines. The crusts should be carefully removed by starch poultices or by softening them with liquid paraffin to which it is often useful to add half a drachm of oil of cade to the ounce, as an antiseptic, and then dilute mercurial ointment should be applied. Boils and furuncles should be opened and swabbed out, but fomentations should not be used as they tend to irritate the skin. The form of eczema which most commonly is complicated by sepsis is infantile eczema of the face.

Eczema in Special Localities.—(1) On the palms and soles. Here the disease is characterised by the formation of deep fissures accentuating the natural lines of the skin and by great hyperkeratosis. This is best treated by the administration of X-rays; if for any reason these are not available tar and salicylic acid are the best drugs to employ. The following is a good prescription—

Acidi Salicylici gr. xv
Hydrarg. Ammon. gr. x
Liquor Picis Carb. ʒ i
Vaseline ad ℥ i.

At night tar and salicylic acid plasters may be applied and the patient should sleep in gloves.

(2) On the scalp an attack of acute eczema gives rise to a very trying condition. The scalp becomes a vast weeping surface, exuding serum which speedily glues the hair together into a sticky mass. It is usually associated with erythematous eczema of the face. The best treatment is to cut the hair short and to clean up the surface frequently with liquid paraffin. Luckily this condition does not usually persist long. It is not very uncommon to find near the nape of the neck a chronic patch of infiltration which often itches very much. Such patches require stimulation and are often very much benefited by painting with a strong solution of nitrate of silver (15 gr. to the ounce).

(3) *Varicose Eczema.*—(See under skin diseases due to circulating disturbances.)

Lichenification.—Persistent patches of eczema often become permanently thickened and infiltrated and somewhat raised above the level of the surrounding skin. At the same time the natural lines of the skin are accentuated and the areas between them stand out clearly, giving the impression of polygonal papules something like those of lichen planus. This condition is known as lichenification and is very persistent. The treatment is often a matter of some difficulty. Sometimes, especially if it has not been previously treated, simple protective measures are sufficient, but as a rule stimulant treatment is required. This may take the form (1) of painting with silver nitrate, (2) of a weak chrysarobin ointment (ten grains to the ounce), (3) painting with tincture of iodine. (4) X-ray treatment, which is by far the most effective method and often succeeds when all the others have failed. Sometimes fairly full doses are required, one-third of a pastille dose once a week for three weeks is about the maximum which is safe, and the surrounding parts should be carefully protected. A few cases which will not yield to X-rays can be cured with radium.

H. D.

PSORIASIS, MOLLUSCUM CONTAGIOSUM, VERRUCA, ACNE

Psoriasis

In the majority of cases an attack of psoriasis will yield to local applications, and a certain amount of benefit also may be obtained from internal medication, but no remedy can be relied upon to prevent recurrence of the disease. The treatment may be considered under the headings of *internal*, *dietetic* and *external measures*.

Internal Medication.—There is no drug which exercises a specific action on psoriasis. Arsenic is commonly prescribed, but, to be effective, it must be given over long periods and in increasing doses, care being taken to avoid toxic manifestations from its continued use. It may be prescribed in the form of Fowler's solution, or the Liq. Sodii Arsenatis. In acute cases, Salicin 15–30 gr. t.d.s., or Salicylate of Soda 10–20 gr. may be administered instead of arsenic. Thyroid gland 1–5 gr. sometimes gives excellent results, but its action is uncertain. Iodide of potassium in large doses has also been advocated, but both these remedies possibly act by causing increased sweating and depression of the general health. I have treated a few cases with intramuscular injections of soamin, salvarsan and enesol (salicylarsinate of mercury); but the results have been disappointing, and this seems to be the general experience. Other drugs which have been found useful are mercury, in the form of the biniodide, antimony, turpentine, carbolic acid and balsam of copaiba.

Diet.—It is doubtful if any special dietetic measures influence the course of psoriasis, but excess of alcohol certainly aggravates the disease. Both a vegetable and a strict meat diet have been tried without any marked effect in ordinary cases, although there are special

circumstances, *e. g.* in obesity, gout, etc., when an appropriate diet, or strict limitation of the food for a short time to meat and hot water, has a beneficial result.

A fact worth remembering in connection with psoriasis is that an intercurrent disease, or a lowering of the general state of health of the patient, is often accompanied by a remission or disappearance of the skin disease.

External Medication.—Better results are undoubtedly obtained from local applications, than from the administration of drugs or from a special diet. Before applying an ointment, the scales must be removed from the patches by scrubbing the skin with soft soap and hot water. A small handful of sodium carbonate may be added to the bath with advantage. Sulphur or tar baths may be substituted. Light, hot air and sea-water baths are also useful. If preferred, natural sulphur baths, obtained at a spa such as Harrogate, Strathpeffer, Aix-les-Bains, Luchon and Schinznach may be tried. The radio-active waters of Bath and Buxton or the arsenical waters of Woodhall Spa, La Bourboule, Levico, etc., are also of service. Patients sometimes lose their psoriasis in tropical countries, and a warm sunny climate should therefore be given the preference.

After the removal of the scales the ointment is rubbed in or spread on lint or linen and held in position by means of a bandage. The most efficacious drug is certainly chrysarobin, but it has the disadvantage of staining the skin and linen and of causing acute dermatitis or conjunctivitis and toxæmic symptoms from absorption if improperly used. In extensive cases it is better not to use this drug unless the patient can be kept in bed under medical supervision. Chrysarobin ointment is applied daily until the skin surrounding the patches shows an erythematous areola. When the reaction has subsided, the process may be repeated. If the patient cannot be kept in bed, chrysarobin may be used for small patches in the form of a varnish, *e. g.*

℞ Chrysarobini ʒ i
Gutta perchæ ʒ i
Chloroformi ʒ x,

or

℞ Chrysarobini ʒ i
Acid Salicylici gr. x
Collodion Flexile ad ℥ i.

Small quantities of the drug may also be combined with ichthyol, ammoniated mercury, tar, salicylic acid, etc., in an ointment, *e. g.*—

℞ Chrysarobini } āā 5
Ichthyol. }
Acid Salicylici 3
Paraffini Mollis 100.
(Unna.)

℞ Acid Salicylici 10
Chrysarobini } āā 20
Olei Rusci }
Saponis Viridis } āā 25.
Paraffini Mollis }
(Dreuw.)

℞ Chrysarobini. } āā gr. x
Hydrarg. Ammon. }
Liq. Picis Carb. ♏ x
Paraffini Mollis ℥ i.
(Hutchinson.)

Pyrogallic acid probably comes next in point of efficacy to chrysarobin, but is attended by the same disadvantages and similar precautions must be taken. It may be used in a 2–10 per cent. ointment or substituted for the chrysarobin in the above prescriptions. Eugallol is a convenient preparation for small areas; it should be mixed with an equal quantity of acetone and painted on the patch, which is then dusted over with powdered zinc oxide.

The most serviceable drug for ordinary cases is tar. In moderate proportions the various preparations of tar do not irritate the skin, and may be used for long periods with safety, but they are unpleasant on account of their dirty brown colour and penetrating odour, and in some patients cause "tar acne." Liq. Picis Carbonis is one of the least objectionable, it may be painted on pure or made into an ointment in combination with others drugs, *e. g.*—

℞ Liq. Picis Carb. ʒ ii
Zinci Oxidi ʒ i
Paraffini Mollis ad ℥ i.

℞ Liq. Picis Carb. ʒ i
Hydrarg. Ammon. gr. x.
Ung. Acidi Salicylici, ad ℥ i.

Oleum Cadini, Oleum Betulæ Alb. or Anthrasol may be substituted for Liq. Picis Carbonis. If Ung. Picis Liq. is prescribed, it should be diluted with soft paraffin or with zinc ointment, and Ung. Glycerini Plumbi Subacetatis. The mercurial preparations such as the ammonium chloride, dilute nitrate of mercury, or the red or yellow oxides of mercury, are often of service, especially for the scalp and face, and in inflammatory cases when tar is badly tolerated. β-Naphthol, resorcin, sulphur or salicylic acid may be combined with them.

X-ray treatment gives rapid and successful results in the majority of cases, although relapses occur as in other methods. It is chiefly indicated in chronic localised patches which resist the action of ointments, but moderately extensive cases may also be treated. Care must of course be taken to protect susceptible organs

and to allow sufficiently long intervals to elapse between each series of exposures. A Sabouraud pastille dose, or half this amount repeated two or three times, is usually sufficient for a single area. There is no definite indication for the use of vaccines, and their indiscriminate employment is unwarranted.

Molluscum Contagiosum

This is a local contagious disease, and the treatment consists in thoroughly destroying the lesions as soon as they are recognised. If they are small and few in number, this can be accomplished with very little pain and without subsequent scarring by squeezing them out with the finger-nails or by enucleating them with forceps and applying a little pure carbolic acid or solid silver nitrate to the base of the tumour. The galvano-cautery or the electrolytic needle may also be used. In children, when the lesions are numerous, an anæsthetic may be required, the tumours can then be incised from below upwards with a small scalpel and the contents squeezed out or scraped away with a small sharp spoon. Pedunculated tumours may be cut off with curved scissors and the base cauterised. This method is suitable when the eyelids, breasts or genital regions are affected. Occasionally the lesions coalesce to form large, prominent suppurating tumours, and these should be scraped or excised under an anæsthetic. It should be remembered that Turkish baths and certain birds such as linnets, pigeons and fowls are a frequent source of infection. Precautions should also be taken to avoid infecting other persons.

Verruca

Warts may be removed by (1) local mechanical or surgical measures, or (2) the administration of certain drugs. The former is, in my experience, the only certain method of eradicating the growths. The value of internal remedies is problematical, but there is good authority for the success of magnesium sulphate, arsenic, lime-water, etc., and one of these drugs may be tried in combination with local treatment. It is possible that the soil may thus be modified so as to make it unfavourable for the development of the growths, but since warts are inoculable, I prefer to use a local antiseptic such as a weak sulphur ointment.

The ordinary wart (verruca vulgaris), which chiefly occurs on the hands and fingers of children, may be dealt with in various ways according to the size, situation and characters of the tumours. When the warts are small, the galvano-cautery or the electrolytic needle (attached to the negative pole of the battery) may be used. If pedunculated, the warts may be snipped off with scissors and a caustic applied, or a tight ligature may be applied to the base of the wart.

For warts of medium size, the application of carbon dioxide snow is a simple and efficacious method of treatment. A pencil of the same diameter as the wart is firmly pressed on the tumour till the latter is frozen through to its base. This process may take from thirty seconds to two or three minutes. Since the horny tissue resists the action of the snow more than the normal skin, too much of the latter should not be included. The application may be repeated if necessary several times, at intervals of a fortnight or three weeks. If carbon dioxide snow is not available, salicylic collodion or plaster or a caustic such as fuming nitric acid, the liquid acid nitrate of mercury, glacial acetic acid, etc., will remove the warts if applied frequently. The skin surrounding the wart should be protected with vaseline and the acid applied on a glass rod. For large single warts, carbon dioxide, ionisation with magnesium sulphate, or radium may be employed, or the growth may be excised. When the lesions are numerous and closely aggregated, X-rays in Sabouraud pastille doses are sometimes successful, but care should be taken to avoid severe reaction, as atrophy of the skin and telangiectasis may ensue several months after the exposure. Multiple flat warts on the face are best treated with an ointment of sulphur and salicylic acid, and the so-called seborrhœic warts of old people sometimes disappear under the same treatment. Individual flat warts may be touched with pure carbolic acid, or a finely pointed stick of carbon dioxide snow. Senile warts often require radium, freezing or X-rays. In senile keratosis occurring in patients who have lived in tropical climates, I have had more success with carbon dioxide snow than with radium or X-rays. In gonorrhœal warts, antiseptic lotions and removal of the lesions by the knife or galvano-cautery is indicated, and post-mortem warts, which are caused by the tubercle bacillus, should be removed by the same means.

Acne

The treatment of acne vulgaris consists in the removal of any predisposing factors adversely affecting the general state of health; the use of various local hygienic measures to check the seborrhœa; the application of antiseptic and scaling lotions and ointments for the removal of the eruptive lesions and, lastly, the employment of vaccines or of surgical and physical procedures, such as incision, the galvano-cautery, X-rays, etc., in inveterate cases.

Internal Medication and Diet.—If anæmia, constipation or dyspepsia are present, iron,

arsenic, aperients, gastric sedatives, etc., should be administered according to the special indication. A mixture of ferric sulphate and magnesium sulphate is often beneficial. Ichthyol 5 gr. in pill or capsule and calcium sulphide ½–2 gr. are often prescribed with good results. Brewer's yeast or one of its numerous preparations is worth a trial. No special diet is indicated, but the patient should avoid rich and fatty foods, and alcohol, tea and coffee should be prohibited or taken in great moderation. Dyspepsia, constipation and dilatation of the stomach, if present, require the diet suitable for these conditions.

Local Hygienic Measures.—These consist in combating the seborrhœa, expressing the comedones, and evacuating the pustules. The face should be steamed or thoroughly washed with soft soap or a medicated soap such as one containing ichthyol 10 per cent., or sulphur, camphor and balsam of Peru āā 5 per cent., and then vigorously rubbed with a rough towel. The comedones should then be expressed by a comedo extractor and an ointment or paste applied.

External Medication.—The most efficacious drugs are sulphur, resorcin and ichthyol. Astringents such as zinc sulphate and the preparations of mercury are also of service.

℞ Sulph. Præcip. gr. x–xxx
Resorcini gr. x–xx
Paraffini Mollis ad ℥ i.

is a useful ointment. If a scaling paste is required, the quantities of these drugs may be increased to 1 dr. and ½ dr. respectively, and a little powdered starch added. During the day, a lotion is more convenient for the patient to apply than an ointment; it may consist of the ordinary calamine lotion to which sulph.-præcip. 10 gr. ad 1 oz. is added or one of the following.

℞ Sulph. Præcip. gr. xv
Glycerini ♏ x
Spirit Rectificat ♏ xv
Liq. Calcis ʒ ii
Aq. Destill. ad ℥ i.

or

℞ Zinci Sulphatis gr. xv
Potass. Sulphidi gr. xv
Aq. Camph. ad ℥ i.

Surgical and Physical Measures.—Pustules and abscesses should be opened with a small scalpel and evacuated, or a little pure carbolic acid may be inserted on the point of a wooden match or by means of a grooved needle. Some authorities prefer the galvano-cautery or a small rotary curette. X-rays in Sabouraud pastille doses are serviceable in certain cases, especially in the deep-seated indurated type, but should not be repeated too often on the face. Bier's suction cups, carbon dioxide snow and diathermy have also been recommended.

Vaccines.—Vaccines are chiefly of value as an adjunct to other measures. An autogenous acne bacillus vaccine, in doses of 5–10 millions and upwards, administered every ten days, when the comedo is the predominant feature of the case, and an autogenous staphylococcus vaccine beginning with about 200 millions, when there is much pustulation, is sometimes productive of good results.

On account of the difficulty of cultivating the acne bacillus and of determining whether the suppuration is caused by a secondary infection of staphylococci or by the acne bacillus alone, a mixed stock vaccine of acne bacillus and staphylococcus is sometimes preferred.

Acne Varioliformis.—This is a rare form of acne which chiefly affects the forehead and scalp and leaves deep pitted scars; it may be treated by sulphur or mercury lotions and ointments in a similar manner to acne vulgaris. In cases which resist this treatment, vaccines or X-rays may be tried.

Rosacea.—This condition is usually classed as a variety of acne, although in many respects it is a totally different disease. Dyspepsia and a sluggish peripheral circulation are the underlying factors. Tea, coffee, stimulants and all articles of diet which cause reflex flushing of the face must be carefully avoided. Internally, a bismuth mixture before meals and ichthyol 5 gr. or menthol ½ to 2 gr., after meals, alleviate the symptoms. When much seborrhœa is present, a sulphur lotion should be applied every morning and a mild sulphur and resorcin ointment at night as in acne vulgaris. Mercurial preparations are also useful when there is much pustulation. Dilated venules on the nose and cheeks should be treated by electrolysis, a fine needle attached to the negative pole being inserted into the vessel and a current of ½–2 ma. allowed to pass for a few seconds. A fine-pointed galvano-cautery burner may also be employed, but the risk of leaving small scars is greater. In the condition of the nose known as rhinophyma, the hypertrophied portions of skin may be shaved off with a scalpel. Scarification, X-rays, radium and carbon dioxide snow have also been used with success. S. E. D.

RODENT ULCER

The ideal treatment for every case of rodent ulcer is to cut it out, employing incisions which leave a wide and deep margin round the diseased tissue. When for one reason or another this plan of treatment is impracticable there are various other alternative measures which may be adopted, and these are often successful;

nevertheless, excision remains the method of choice. The following are the chief reasons which forbid excision. (1) The large size of the ulcer, which may render it impossible to close the wound satisfactorily. (2) The position of the ulcer. If, as is frequently the case, the ulcer is situated near the eye, possibly involving the lids, or the mucous membrane, an operation may cause grave deformity. (3) The reluctance of the patient to submit to surgery.

In default of excision the following are the principal methods of dealing with rodent ulcer: (1) X-rays, (2) ionisation, (3) carbon dioxide snow, (4) radium, (5) caustic pastes.

In most cases good results can be obtained by these methods, but under certain conditions rodent ulcers may be very refractory to treatment. These conditions are: (1) When the ulcer is of a very large size. (2) When it has attacked and begun to destroy either mucous membrane, cartilage or bone. (3) When it has recurred after apparent cure. If a rodent ulcer has been apparently cured with X-rays or radium but subsequently recurs it is always much more difficult to treat successfully.

1. X-rays.—Very satisfactory results can often be obtained by the use of X-rays. They are particularly effective in obtaining the speedy healing of ulceration although they often leave, after healing has taken place, nodules of new growth round the edge. These are sources of danger because they may at any time break down with the formation of new ulcers. In administering X-rays to a rodent ulcer it is permissible to give fairly full doses, provided, of course, that care be taken to protect the healthy skin. A good plan is to give a pastille dose once a week for three weeks and then to wait for three weeks to observe the result. In cases where there is a rapid extension of ulceration it is legitimate to give much larger doses than this; in fact, a radiologist of great experience once told the writer that in the case of a lady where ulceration was rapidly destroying the ala of the nose he had given as much as four pastille doses at one sitting with excellent results. Such heroic doses as this should, however, be reserved for great emergencies. The beads or nodules of growth that may remain after the ulceration has been healed up will ultimately yield to repeated doses of the rays, but they are most conveniently dealt with by employing the carbon dioxide pencil. The pencil should be applied with firm pressure for about forty seconds to each nodule in turn. The reaction is often severe, but it begins to calm down after about four days and the scar left is almost invisible.

Another plan is to combine X-rays with a preliminary curettage of the ulcer. This method of procedure has the advantage of clearing away at once the superficial disease and leaving the deeper parts well exposed to treatment. It therefore saves much time. In this plan the doses of X-rays given may be much smaller, a pastille dose every three weeks until healing is complete.

2. Good results have been reported by many observers from the use of ionisation, which has the merit of needing only simple apparatus. A battery of galvanic cells, zinc electrodes and conducting wires are all that are absolutely necessary, although it is interesting to have also a milli-amperemeter to measure the current actually being used.

As zinc is a metal which moves from the positive to the negative pole in the external circuit of the battery the positive pole is applied to the ulcer. This is composed of the solid zinc electrode applied to a pad made of several thicknesses of lint soaked in a 2 per cent. solution of zinc sulphate. Care must be taken that pressure is even over the whole area treated as otherwise the treatment will be much more painful, and the current will be concentrated to one or two points which will be burnt, while the remainder of the ulcer will not be treated at all. If these precautions are taken as strong a current may be used as the patient will bear. The length of a sitting should be about ten minutes, and at the end of this time the ulcer will be found to be whitened. After a few days a scab forms, and when this falls off the ulcer will be found to be partially if not completely healed. The process is repeated until healing is complete. Recurrences are not uncommon after ionisation.

3. Carbon Dioxide Snow.—This is one of the most recent additions which has been made to the methods of dealing with rodent ulcers. It is most useful when used as a subsidiary to X-rays as described above, but small ulcers may be successfully treated by its means alone. It has the advantage of being cheap and very easy to use. A pencil, made to the exact size of the area which is to be treated, well protected by a double layer of lint, is grasped between the finger and thumb and applied with firm pressure. The time of application may be as much as a minute and half or even two minutes. It is not very painful except when the pencil is pressed upon bone lying immediately beneath the skin. In that case a good deal of painful periostitis may be set up. For a rodent ulcer which already has invaded bone or cartilage this method is useless. After the employment of carbon dioxide snow there is always considerable reaction with the outpouring of serum and the subsequent formation of a crust or scab. It takes from ten days to a fortnight, according to the length of time and pressure used, for this crust to separate. The scar left

is always smooth and pale, but if the snow has been used with sufficient vigour to cause considerable loss of tissue, it may be somewhat depressed. Snow has this advantage, that it is just as effective in dealing with recurrences as with the primary growth. In this respect it is unlike, and superior to, X-rays.

4. Radium is extremely effective in dealing with rodent ulcers. It has, moreover, the advantage that it can be applied to situations which are almost inaccessible to X-rays.

Radium and X-rays are somewhat similar in their action, but they are by no means identical. There is always a reaction after the use of radium which begins about three days after its use. There is no reaction after the use of X-rays unless an over-dose has been administered, and then a troublesome dermatitis may result. Moreover, radium has the advantage that it will sometimes cure ulcers which are refractory to X-rays, or which have perhaps yielded to X-ray treatment up to a certain point and then remained stationary. A further advantage of radium is that owing to the small size of the apparatus required it can be employed in situations which are inaccessible to X-rays, the apparatus for the administration of which is necessarily somewhat cumbersome.

For the treatment of all lesions on the skin, both rodent ulcers and other conditions, it is essential to use a flat applicator with which it is possible to get an even radiation over an area equal to that of the apparatus. It is usual to spread the salt upon a metal plate and to cover it with a layer of varnish in order to protect it against organic fluids. This layer of varnish cuts off the softest rays. Such applicators are conveniently fitted at the back with a handle to facilitate their manipulation. The applicator is kept in position by means of a strip of zinc oxide plaster. In treating rodent ulcers large doses are used. Applicators of full strength are applied without screens to the surface of the growth and left in position for about an hour and a half at a time. The full therapeutic effect of a dose is not seen until six weeks after its administration. A small rodent ulcer may be cured in one sitting, others require several, and some are quite refractory. These last, however, are usually either very large and deep ulcerations or they are recurrences.

5. The application of caustics to rodent ulcer is an old method of treatment which is now out of fashion, although cases arise from time to time in which it proves useful. The use of these agencies is best combined with that of the curette. The patient is anæsthetised and as much as possible of the disease is scraped away and then the paste is applied. That which is perhaps the best is an arsenic paste containing 5 per cent. arsenious acid. A case was shown at the Dermatological Section of the Royal Society of Medicine recently in which a remarkably good result had been obtained by means of this compound. A man who had suffered from rodent ulcer for twenty years, in whom the disease had extended both widely and deeply, was curetted twice with an interval of ten days between the operations and each time treated with this paste. It was extremely painful and caused an apparent extension of the ulceration; dressings of 2 per cent. formalin were subsequently employed and complete healing, interrupted only by the exfoliation of some dead bone, took place. The constitution of arsenic paste is as follows: Arsenious acid and gum arabic one part each with ten parts of talc to which sufficient water is added to make a thick paste. H. D.

LUPUS ERYTHEMATOSUS

In the treatment of lupus erythematosus it must be borne in mind that the eruption is in all probability the expression of a general state. What exactly that state is, whether it is due to a circulating toxin, or to some unknown bacterial infection, or to some metabolic disturbance, must for the present be left in doubt. It is, therefore, important to remember that the removal of the local lesions by local applications is not necessarily a cure, and it will be well not to promise too much to the patient. In almost every case the eruption returns after a longer or shorter interval even when it has been entirely removed, and in a large proportion of cases the most strenuous treatment only results in a moderate improvement. The prognosis, therefore, is not favourable even in a mild case. One is constantly hearing of some new measure which will cure the disease, but a little experience proves that it only removes for a time the local expression of the general condition. (It is hardly necessary at this time to insist that lupus erythematosus has no relationship to lupus vulgaris.)

It is convenient to note that there are two distinct types of lupus erythematosus, and many intermediate conditions.

Chronic Type.—The most common type is characterised by its chronicity, by the slow growth of the lesions, which are usually placed symmetrically on the flush areas of the cheeks, often extending across the bridge of the nose, in butterfly or bat's wing form. In some instances the nose is the first part attacked, and the disease may spread from it on to the cheeks. The auricles are frequently affected, and also the scalp. The lesions are usually well-defined, slightly raised and covered with scales. In cold weather chilblain-like lesions

are common on the fingers, especially on the dorsal aspects and on the inner sides of the hands. In some cases there is a condition of the fingers resembling Raynaud's disease.

A history of some previous tuberculous disease, *e. g.* glandular abscesses, bone or joint disease, may be obtained, and a family history of tuberculosis is common. At present we are unable to say if tuberculosis plays any part in the etiology of lupus erythematosus, and there is much evidence against this hypothesis. The patient usually complains of cold extremities, and the eruption is usually worse in the winter and spring months.

General Treatment.—The patient should be well fed, milk, cream and other fatty foods being given in excess, if they can be properly digested. Where possible a residence in a dry climate is to be recommended, cold and damp being specially favourable to the development of the disease.

Drug Treatment.—The most satisfactory remedy internally is certainly quinine, beginning with three to five grains three times a day, and if this is well tolerated it may be continued for a long time. Salicin, in fifteen to twenty grain doses three times a day, in cachet or in a mixture with a little syrup of orange, is also of value, especially in the early cases. Ichthyol in doses of five grains or more three times a day, in tablet or capsule, may also be given with advantage. In some cases general tonic treatment by iron and arsenic will be found beneficial. Tuberculin injections have no influence on the condition.

Local Treatment.—In the circumscribed forms the application of the carbon dioxide stick for ten to twenty seconds, or painting with carbon dioxide snow dissolved in ether, acetone or alcohol is very useful. An inflammatory reaction follows the application, and a scab forms which on removal leaves a smooth surface. The applications may be repeated after an interval, and sometimes several months' remission may be obtained.

Painting the area with tincture of iodine daily for several days will often give a satisfactory result, the scaly mass peeling off and leaving a smooth surface. Pure medicinal cyllin may be similarly used. In both these treatments there is temporary disfigurement owing to the brown staining of the parts, and the patient will have to remain indoors.

Salicylic plasters applied for forty-eight hours at a time will also remove the dry scaly plaques which are commonly seen.

Radium applied on a flat applicator for short periods, say half an hour, often gives gratifying results, but of course the treatment is expensive.

The Finsen light is rarely applicable to lupus erythematosus.

It is essential that treatment of this type is to be reserved for the chronic lesions, and the remedies above mentioned are not suitable for the early or more erythematous type of case. If they are used there is great risk of increasing the area of the disease. I have seen this in a number of instances. In these early cases soothing applications such as the liniment of calamine are indicated.

However good the result from local treatment, the probability of recurrences must be remembered, and it is wise to warn the patient of this. Even when the disease has disappeared as a result of a prolonged residence in a warm, dry climate, relapses may occur on returning to a damp, cold environment.

Acute Type.—The acute type of lupus erythematosus is comparatively rare. It occurs almost exclusively in young girls and young women.

It is characterised by an acute outbreak of erythematous patches on the flush areas of the cheeks, on the backs of the hands, elbows, knees, and sometimes on the trunk. There is often fever, and the prognosis is sometimes very grave. There may be visceral complications, nephritis, pneumonia and pulmonary or glandular tuberculosis.

In this type, the patient must be kept at rest, and fever and other complications are to be treated on the usual lines. Quinine in large doses (five or more grains thrice daily) is the only remedy which has any effect on these acute cases, and sometimes its effect is remarkable. Salicin in large doses (twenty grains and upwards thrice daily) also appears to have a distinct influence, but is inferior to quinine. Locally, the best application is a soothing lotion, such as the liniment of calamine (calamine 35 gr., Ol. Olivæ ½ oz., Aq. Calcis ½ oz.), frequently applied.

In some intermediate cases and in all early cases it will be found better to treat by such soothing local applications, reserving the more drastic applications mentioned above for the chronic type of the disease. J. H. S.

THE TUBERCULIDES

The name "tuberculide" is applied to a group of skin eruptions occurring in tuberculous subjects, and believed to be caused by the circulation in the blood of tuberculous toxins developed at a glandular or other focus, or by decadent forms of the tubercle bacillus brought to the skin by the blood-stream from a distant focus.

For practical purposes, we may divide them into three classes. (1) A papular eruption called Lichen scrofulosus. (2) A group of papular and nodular eruptions, tending to

necrosis, which may develop in the true skin and sometimes round the hair follicles. (3) Chronic indolent swellings in the subcutaneous tissue tending also to necrosis.

1. **Lichen scrofulosus** is of little clinical importance beyond being an evidence of tuberculosis. The lesions are round, reddish or reddish-brown papules the size of a pin's head to that of a millet seed, occurring in groups on the trunk. They are most common in children suffering from tuberculous adenitis, bone or joint disease, and they occasionally occur in lupus vulgaris. They cause no symptoms, and, beyond the general treatment required for the tuberculous process of which they are an evidence, rarely require treatment. Local inunction of cod-liver oil has been advocated.

2. **Necrotic Tuberculides of the True Skin** may be follicular or non-follicular. They occur symmetrically on the extremities, particularly on the backs of the knuckles, wrists, elbows and the fronts of the legs. Occasionally, they develop on the outer edges of the pinnæ of the ears, and rarely elsewhere. The lesions vary in size from that of a hemp-seed to a small pea, are hard to the touch at first, purplish or purple-brown in colour, and are associated with a bad peripheral circulation, chilblains and acro-asphyxia. They run an indolent course, and tend to necrose in the centre, where small ulcers form, which take a long time to heal. They invariably leave scars, and when the auricles are affected, may cause definite atrophy or distortion. They are associated with some tuberculous focus, glandular or other, and the general treatment for all such conditions is indicated. Plenty of good food, milk, cream, cod-liver oil and general tonics are indispensable. The extremities should be protected as far as possible from cold, warm water should be used for washing and flannel should be worn. Small doses of tuberculin have been recommended, but as a rule the general treatment above indicated gives good results. Where there is ulceration, the parts should be dressed with a stimulating antiseptic ointment, such as the Unguentum Hydrargyri Oxidi Rubri. Residence in a warm, dry climate, if it can be obtained, is of the highest value.

A number of names have been given to this form of tuberculide—folliclis, acne scrofulosorum, acnitis, etc., dependent upon the local characteristics of the lesions.

3. **Tuberculides of the Subcutaneous Tissue. Bazin's Erythema Induratum.**—Bazin's disease occurs almost exclusively in young girls, particularly in those who have to stand a good deal at their work. It is bilaterally symmetrical, the individual lesions being indurated red or purplish swellings rather resembling gummata, found most frequently on the calves and sides of the legs. The swellings usually run a very chronic course, and sometimes disappear without ulceration.

In most cases, however, necrosis of the centre of the lesion occurs and a deep, indolent ulcer forms. On healing, a depressed cicatrix is left.

The essential for successful treatment is rest of the limbs in the horizontal position, and, if this can be carried out, the ulcers mostly heal in about three weeks. If ulceration has not yet occurred, the swelling may entirely subside while the limbs are rested.

The ulcers require a stimulant antiseptic ointment, such as the Ung. Hydrarg. Ox. Rubr., and short exposures to X-rays equivalent to half a pastille dose at intervals of a week.

The resting of the limbs is supplemented by good food, cod-liver oil and other tonics. Minute doses of tuberculin are recommended by some clinicians, but I cannot say I have been favourably impressed in the cases in which I have tried it.

In many cases, unfortunately, when the patient returns to work, especially if that involves prolonged standing, and if her nutrition is not well maintained, relapses are likely to occur. Ultimately, the patient usually recovers, but the cicatrices persist, and are often mistaken for the scars of syphilitic gummata.

J. H. S.

PRURITUS

Pruritus is the *sensation of itching.* All the cutaneous sensations are protective with the exception of pruritus, which is injurious inasmuch as it is followed automatically by scratching. The sensation may be excited in a perfectly normal skin, but when it occurs spontaneously it is almost invariably symptomatic of some abnormal condition of the epidermis. Essential pruritus as a pure neurosis arising from spinal irritation is an extremely rare disease. The peripheral changes which provoke the sensation are, broadly speaking, œdema of the epidermis, and irregular distribution of the lymph and blood. The œdema leads to softening of the epidermic cells and imperfect cornification, and, in consequence, to a lowering of surface pressure. This lowering of surface pressure is invariably accompanied by a tendency to pruritus. Of predisposing causes the most important is hyperæsthesia, and therefore whatever leads to hyperæsthesia tends to induce the pruritic state. The frequency with which the pruritic state occurs varies in the different decades of life and in the different races of mankind. Children in the first few years of life who inherit a tendency to asthma and eczema often suffer from hyperæsthesia of the skin, and consequently from pruritus which almost invariably leads to eczema. Pruritus is less

commonly met with in early adult life, but there is a marked increase in its occurrence at the climacteric period, both in men and in women. Some of the worst forms of hyperæsthesia of the skin are the result of long-continued nerve strain and worry. Not unfrequently it accompanies senile degeneration of the skin.

Clinical Types of Pruritus.—A sharp distinction can be drawn between those cases of pruritus in which the sensation arises now in one area and then in another all over the body, and those in which it is confined to one small area such as the anus or the genital organs.

1. *Generalised Pruritus.*—The great majority of cases of generalised pruritus are due to some definite causation such as animal parasitic infection, or food poisoning, and no case must be diagnosed as a neurosis until these diseases have been excluded. The events which lead to a general pruritic condition of the skin are: (1) the saturation of the epidermis and follicles with fatty bodies (Seborrhœa). (2) Neurasthenia producing sensory hyperæsthesia. (3) Senile atrophy of the cutaneous tissues. Some cases of generalised pruritus seem in some way connected with temperature, certain individuals suffering during the winter months (P. hyemalis) and others only in hot weather (P. æstivalis).

2. *Local Pruritus.*—The regions most liable to suffer are the scalp, the anus and perineum, the scrotum and vulva and less frequently the palms and soles. Pruritus of the scalp, when not due to animal or vegetable parasites, is almost invariably due to seborrhœa.

Pruritus of the Anus and Perineum is a common affection in middle life. Its causation is intimately associated with the circulation through the hæmorrhoidal and portal veins. The slowing down of the blood current in these veins and the tendency to stagnation is followed by a lateral escape of lymph into the perineal epidermis with consequent lowering of surface pressure. From this to the formation of minute epidermic fissures is but a step in the downward course of degeneration, and the invariable consequence is pruritus, especially troublesome to the patient when in bed. The unavoidable scratching by which relief is sought, leads to the formation of eczema, hence long-continued pruritus ani is usually accompanied by more or less inflammation.

Pruritus of the Vulva and of the **Scrotum** may be due to the same causes as those which lead to pruritus ani, but in some cases it is a purely reflex phenomenon due to some pathological disturbance in neighbouring tissues, for example, a caruncle or ulcer of the urethra (Gibbons), or a varicose condition of the rectal veins. Pruritus vulvæ is not uncommonly met with in women who are passing through the climacteric period. It may be provoked by irritating discharges, by diseases of the vulva, or by reflex irritation. The worst and most intractable forms of pruritus vulvæ are those which are associated with atrophy of the labia and clitoris (Kraurosis).

Treatment of Pruritus.—The first step towards the successful treatment of any case of pruritus is the discovery of the causes which lie behind the cutaneous irritation. This requires a careful examination of the individual and his surroundings, and also of the entire cutaneous surface. No case must be diagnosed as a neurosis until all possibility of scabies, of pediculosis, or of urticaria have been excluded. Each of these diseases being accompanied by definite and characteristic symptoms, no real difficulty should prevent a correct diagnosis. Many cases of general pruritus from which these causes have been excluded exhibit a general blocked condition of the follicles from accumulation of secretion, and these cases are apt to be accompanied by pruritus, when the cutaneous stagnation is accompanied by intestinal or hepatic stagnation. The line of treatment indicated in these cases is the free use of soap and water. If the skin is greasy the application at night of an ointment containing 2 drachms of sulphur to an ounce of vaseline is useful. When the follicles are thickened and blocked a solution of salicylic acid 8 gr. in an ounce of spirit and water is indicated. The following lotion is of great value in the treatment of pruritus of the groins due to retention of secretions without inflammatory symptoms.

Sodæ bicarb. gr. x
Phenolis gr. x
Glycerini Amyli ♏ v
Sp. Vin. Rect. ʒ iss
Aquam Destill. ad ℥ i.

The lotion must be painted on the parts two or three times a day, and the affected areas well dusted over with Fuller's earth.

Treatment of Pruritus of the Anus and Perineum.—Excluding children, in whom this affection is nearly always due to intestinal worms, pruritus ani is generally met with in adults. A careful examination of the parts will almost invariably reveal, even when there is no eczema, an œdematous condition of the epithelium and the presence of one or more minute fissures lying at the bottom of the anal folds. As this œdema is the result of a constitutional tendency to venous stagnation, the pruritus is apt in these individuals to be more or less chronic, disappearing for a time, only to reappear when the patient is depressed or run down. The treatment is both general and local. Any remedial measure which tends to invigorate the individual will do good; hence change from a depressing to a bracing climate has a favourable

effect. Brain rest and freedom from worry are strongly indicated. A tonic containing nux vomica and acids with gentian is an excellent restorative. Local treatment must aim chiefly and foremost at producing a drier condition of the epidermis and hence raising the surface pressure. For this reason fatty ointments should, for the most part, be avoided. If the patient is generally hyperæsthetic, a solution of silver nitrate (2–5 gr. to the ounce of distilled water) is a safe lotion to begin with. It must be applied deliberately *between the folds* of the anus and some inert powder dusted over. Usually the remedy is too mild, and we have to fall back on tar or a solution of tar in spirit. Pure undiluted liquor carbonis detergens or liquor picis carbonis may be used, but Leistikow's formula for Tinctura Lithanthracis has been the most useful in my hands. An excellent alternative to these forms of tar is liquor rusci detergens or a solution of oleum rusci in spirit. In cases in which the spirit disagrees crude coal tar itself may be applied. None of these tar preparations must be used for a longer period than four or five days at a time, and they should be followed by *negative* treatment such as zinc gelatine, or Lassar's paste continued for twenty-four to forty-eight hours, after which the tar may be resumed. In the worst cases, in which we have to deal with morbid hyperæsthesia or with neurasthenia, the most sedative effects are obtained by radiant energy. One or two exposures to the X-rays of the affected parts may be successful when all chemical agents have failed. A half Sabouraud dose may be given at the first exposure, and if not successful a full dose three or four days later. Of radium in the treatment of pruritus I have had no experience, but Mr. Hayward Pinch of the Radium Institute says that it is undoubtedly of great use in pruritus, but "when no actual lesions exist and the trouble is purely nervous in character the results are not so satisfactory and often little benefit follows the application." The use of cocaine ointment in the treatment of pruritus of the anus and of the genitals should rather be avoided than encouraged. It may temporarily deaden the sensation of itching, but has no curative effect. In intractable cases of pruritus vulvæ where there is reason to believe that organic degeneration of the nerves or nerve-ending of the labia has occurred, the only remedy may be complete excision of the external genital organs.

H. L.-R.

PRURIGO

Many different affections have received this name. It is not unfrequently confused with pruritus, as when, for example, an itching papular eruption is described as "pruriginous." The confusion arises from ignorance of the phenomena which alone ought to be included under the name Prurigo.

Prurigo is a disease with very remarkable features which were first clearly delineated by Hebra. It is characterised by intolerable itching and by the formation of small papules on the trunk or limbs. The papules are recognised by touch rather than by sight, at least in their early stages. They are at first of the same colour as the skin and are situated below the level of the epidermis. They are always isolated, and cause great irritation. They provoke violent scratching, which gives rise in turn to various secondary events, excoriations with hæmorrhage and formation of blood scabs, eczematisation of the skin and local septic infection. A remarkable gradation is observable in the number and severity of the lesions as we proceed from the scalp downwards. While the scalp and face are free, or only slightly affected, a few lesions are scattered on the chest, increasing in number on the abdomen. In a well-marked case the maximum number of lesions occur on the buttocks, thighs and legs. When the disease has lasted for some time the skin gradually becomes pigmented, coarse, rough and scaly, and may present an accidental resemblance to ichthyosis. When much eczema or ecthyma is developed the nearest lymph glands will become enlarged. This enlargement is especially marked in both groins, forming the so-called "prurigo-buboes."

The course of the disease is very chronic, often lasting a lifetime. Some abatement in the severity of the symptoms is noticed during the summer months. Various degrees of severity are met with, not only in different individuals, but in the same person during different periods of his life.

Prurigo begins in childhood, and is more frequently met with in boys than in girls. The subjects of the disease are poor and ill-nourished and often of low mental organisation. According to Hebra it is not congenital.

The treatment of prurigo is very unsatisfactory. The most that we can do is to mitigate the patient's sufferings, but experience shows that as soon as we cease treatment he relapses into the pruriginous state. When possible the patient's food and general surroundings should be improved. A warm bran bath with soap taken daily brings a measure of relief. Our efforts should be directed to softening and removing the diseased layers of epidermis. A serviceable ointment is afforded by salicylic acid, thus—

Ac Salicylici ʒ i
Vaseline ad ℥ i.
(m. q. s.).

With this the entire body and limbs are anointed morning and evening. The efficacy of the ointment is increased if it be applied on muslin and secured by a bandage. During the treatment the patient should be immersed in hot water for half to one hour before going to bed, and the body washed with soap. All traces of the soap must be removed before the application of the ointment.

After a period of four or five days of this treatment it is advisable to submit him to the influence of tar. The following formula may be recommended—

Ol. Lithanthracis ʒ ii
Adipis Lanæ Anhydrosi ad ℥ i
(m. q. s.).

This, or any other tar which the physician may prefer, should only be used for a short period at a time. It is advisable to use the salicylic and tar ointments alternately. If suppuration is a feature of the disease tar is contra-indicated. Salicylic acid and ammoniated mercury should be employed until the pus has disappeared. In some cases it is better to apply the tar in a liquid form, thus—

Ac Salicylici gr. viii
Hydrarg. Perchlor. gr. i
Ol. Ricini ♏ x
Tinct. Lithanthracis ad ℥ i
(m. q. s.).

This should be painted on the irritable parts two or three times a day and well dusted over with Fuller's earth. After a period of this the patient should return to the salicylic ointment.

H. L.-R.

SKIN DISEASES DUE TO CIRCULATORY DISTURBANCES

In certain skin diseases the element of vascular disturbance seems predominant, and some of the chief examples of such disorders are conveniently here described. It is not to be inferred, however, that the pathology of the conditions noted is claimed to be purely in the nature of circulatory disturbance.

Chilblains

Chilblains are frequently associated with deficiency in hæmoglobin, and the subjects stand commonly in need of general tonic treatment besides. All measures to improve the general condition, super-alimentation, exercise and the internal administration of iron or other hæmatinics are to be advocated. Ichthyol is of value, but the calcium salts—lactate or chloride—are often disappointing in their action. The hands and feet, which are most commonly attacked, should be washed regularly in tepid water and special attention paid to the drying of them. Socks or stockings should be changed daily, and if circumstances (*e.g.*, perspiration through unwonted exercise) demand it, oftener. Gloves should be worn loose, and should be woollen, or at any rate woven. Leather gloves, save the soft suede variety, are not as a rule desirable.

Local treatment will vary according to the degree of the affection. When dealing with unbroken chilblains, stimulating lotions, liniments, or ointments are admissible. Such a formula as the following—

℞ Ammon. Chlor. ʒ iv
Ac. Hydrochlor. Dil. ʒ i
Spt. Vini Rectif. ℥ i ss
Aq. Destil. ad ℥ iv.

will be found efficacious. Solution of hydrogen peroxide, alcoholic solution of iodine, the ordinary compound camphor liniment, belladonna liniment, ointments containing ichthyol, tar or iodine are all useful on occasion. Should the lesions be cracked or definitely ulcerated, the treatment must necessarily be different. It is generally recommended to deal with ulcerated chilblains on ordinary surgical lines, but a word of caution is necessary in this respect. If strong antiseptics be applied, healing is not only retarded but the lesions are often made worse. The mildest possible applications prove most successful. Amongst ointments Ung. Cetacei is by far the best. A softened Ung. Zinci Oleat. or Ung. Plumbi Subacet. are useful alternatives. Occasionally it may be necessary to apply boric fomentations as a preliminary to ointment, but beyond this it is rarely required to go.

For unbroken chilblains, and for the condition of acro-asphyxia which so many of the subjects of this affection have, electrical treatment gives great and immediate relief. The exact form of current applied does not seem to be of prime importance; either the interrupted or constant application will be found of use. When cracks or ulcers are present, this method is inapplicable.

Note.—For Raynaud's Disease, see "Diseases of the Vasomotor System."

Granulosis Rubra Nasi

This condition of hyperidrosis of the nose, with redness and formation of tiny red papules occurs often as a familial disease. It is associated with tendency to chilblains, and a hyperidrosis of other parts of the body, notably the upper lip, chin, palms and soles. The lines laid down for ameliorating the general condition in chilblain subjects are to be followed, and locally good results may be obtained by repeated short applications of carbon dioxide snow or resorcin paste of medium strength. Marked benefit is

also seen from X-ray treatment. Soon after puberty the condition begins to retrogress, and ultimately will practically clear up, even if no treatment be undertaken.

Urticaria

In embarking upon the treatment of any urticarial condition the practitioner should remember the very numerous causes of this condition. All possibilities in the way of external irritation, parasitic or otherwise, should be investigated and excluded. Acute cases often depend upon gastro-intestinal irritation, traceable to ingestion of some particular food, repetition of which is to be avoided. In children the variety known as Urticaria Papulosa is almost always due to the presence in the dietary of certain articles of food to which the child displays an idiosyncrasy. Generally, sugars in excess, chocolates, malt preparations, gingerbread, bananas or potatoes will comprise the offending material, and trial by elimination will readily enable a persistent Urticaria Papulosa to be referred to its special cause and cured. Large doses of sodium bicarbonate will cut short the attack in children and locally lotions of carbolic acid, liquor carbonis, hamamelis or the calamine liniment, following an alkaline bath, give much relief. In the adult it may be necessary to remove disturbing food factors by emetic or purge, and a saline is preferable as a purgative. Salol in small doses with Mist. Purg. Alb. is a favourite and useful remedy. The more chronic cases not referable to any particular indiscretion in diet may be tried on calcium salts internally. The chloride in large doses—20 to 30 gr.—though somewhat unpleasant to take, is probably the best.

Soured milk or any of the ferments in tablet or powder form, such as lactobacilline, at times are of great service. Yeast or some of its preparations, such as ceridin in pills, or cerevisine powder, have succeeded when other remedies have failed. Ichthyol is disappointing as a rule in the treatment of urticaria. Atropine given in the classical mode of a pill at bedtime relieves irritation, but is not often successful in producing a permanent cure.

Locally much relief is experienced when sulphur and alkaline baths are taken in alternation, and the use of antipruritics, as the tars and phenol, is necessary in severe cases.

The most distressing cases are those of a very chronic nature where the loose connective tissue areas are involved—the so-called Urticaria Œdematosa. Here the internal exhibition of quinine or one of the yeast preparations is most often of use. The possibility of infection of the renal tract by the colon bacillus, or of there being some infection of the biliary channels, should always be borne in mind in these cases,

Varicose Eczema and Ulcer

The so-called Varicose Eczema—a dermatitis occurring in the legs when there is venous stasis, even if varicosity be not marked—is one of the commonest and most troublesome skin conditions. It is unfortunately too often allowed to pass into the state of ulceration, for slight trauma will speedily determine the formation of an ulcer in an eczematous limb. Certain general indications in the way of treatment naturally hold good for both dermatitis and ulcer. The first and most important is rest. If the patient can do so, absolute rest in bed is to be recommended. If this be not possible, then the patient should recline for a stated period each day. Avoidance of standing in one position is to be counselled, as movement is really not so prejudicial as prolonged standing. Support of the limb in all cases by a suitable bandage or elastic stocking is to be advocated. On the whole the crépe bandage for cheapness and general utility is the most universally applicable. It has the virtue, moreover, of being readily cleansed without appreciable damage to its properties. Unna's Zinc Gelatine applied directly to the leg and covered with cotton wool, or locally applied with bandages, is also of great value. It is necessary, of course, that the crépe or other bandage adopted should be worn constantly, and its use should not be dispensed with on the disappearance of the dermatitis. Further, it should be applied before the sufferer gets out of bed in the morning and should not be removed until she retires at night. If the leg becomes painful under the bandage, this must be taken as a warning to recline, and the discomfort must not be relieved by loosening the bandage. Perfunctory applications and the use of inadequate bandages require to be constantly guarded against. Carefully fitted elastic stockings are often of great value, particularly where the patient's circumstances allow of their frequent adjustment and replacement.

In slight and early cases of eczema, in addition to the supporting bandage and the rest, a simple calamine lotion or calamine liniment may be applied. More advanced cases often do well under zinc oleate ointment to which has been added an equal quantity of soft paraffin. If there be much exudation, a simple paste may be indicated, such as Lassar's paste without salicylic acid.

In the treatment of varicose ulcer much ingenuity may be exercised and there is choice of many methods. Careful attention to detail and persistence in carrying out whatever mode of attack be determined upon are of more importance than the special method adopted. Rest and adequate support to the limb are even more essential than when there is dermatitis

alone to be dealt with. If rest in the horizontal position be obtained for a sufficient length of time, any simple antiseptic dressing will usually suffice in the long run to heal the ulcer. Cure may need to be hastened by stimulating ointments, such as the old Ungt. Resinæ or the newer Scarlet Red (5 per cent.) ointment spread upon dressing cloth slightly smaller than the wound area and applied only for a day at a time with alternations of some blander preparation, such as boric acid or zinc oleate ointments. Red wash containing 2 grs. of zinc sulphate to the ounce may be used in a similar way, and the old-time method of stimulating with copper sulphate is not to be despised on occasion when the ulcers are indolent. Unna's zinc-gelatine dressing, used in what may be termed the interstitial method, is almost universally applicable. The ulcers are cleansed as far as possible and then filled with dusting powder, *e. g.* boric acid, dermatol or some one of the numerous iodoform substitutes. Then the leg is bandaged with a gauze or muslin bandage and the hot jelly brushed on and into the bandage. Another bandage is now firmly applied, and finally a third protective bandage put on. The dressing may remain in place for some days or even weeks. Usually, however, it is wise to re-apply it at least each week. It has been suggested that an advantage may be gained by cutting a window in the dressing so that the ulcer may be more often dressed; but experience shows that quite good results are obtained without this device. Even if there is much suppuration no harm usually arises, as the pus finds ready vent beneath the dressing. For economic reasons, many patients must go about, and the doctor is called upon to treat them as best he may. For these ambulant cases no method offers such satisfactory results as the Unna's zinc-gelatine dressing.

When the ulcer is healed, it is well to apply further zinc-gelatine dressing for a period, and later to insist on the use of crépe bandages or elastic support of some kind.

Strapping the ulcer with rubber plaster is an old and sometimes useful device. The intolerable pain of neglected ulcers may be alleviated in the first instance by an ointment composed of equal parts of Ungt. Ac. Carbol. and Ungt. Zinci Oxid. This should, however, be only a preliminary to more thorough treatment. Skin grafting may be necessary in some cases where the areas involved are large.

Internally calcium lactate and calcium iodide are often given in these conditions and sometimes with beneficial results. The general condition of the patient should be inquired into, and diuretics, aperients or cardiac tonics are frequently found to be indicated. It is certain also that although only a small proportion of patients can be definitely proven to have any syphilitic history or reaction, yet the internal exhibition of mercury is one of the most satisfactory procedures in the treatment of both varicose eczema and ulcer.

R. A. B.

TREATMENT OF DISEASES OF THE NERVOUS SYSTEM

EPILEPSY

Definition.—Epilepsy is a morbid state characterised by the recurrence of sudden transient seizures attended with loss of consciousness and often accompanied by evidence of disturbance of cerebral function—motor, sensory, or psychical. These seizures or " fits " are apt to occur in a paroxysmal manner at irregular intervals.

Epilepsy may be associated with gross organic lesions of the brain (tumours, abscess, syphilitic lesions, encephalitis, vascular lesions or trauma), or with obvious defects of cerebral development —organic epilepsy. In these instances it must be regarded as a complication of the original lesion rather than as a primary condition, and its treatment must of necessity be dependent partly upon that of the causal condition.

Epilepsy may arise as an hereditary complaint, without any definite sign of organic cerebral disease, or, on the other hand, develop insidiously quite apart from any hereditary taint or sign of cerebral defect—idiopathic epilepsy. In some cases a reflex factor may be present as a source of irritation, and such cases are known as reflex epilepsy.

Idiopathic Epilepsy

Idiopathic epilepsy—that is, epilepsy arising apart from gross cerebral conditions—may be regarded as a disease, but we are far from understanding its fundamental causes. It is better, perhaps, to consider it as a state or condition characterised by an abnormal instability of the cerebral centres, possibly due to ill-regulated chemical action. This instability may be hereditary, inherent or acquired, and if one grants its existence it is obvious that any disturbance of the psychical or physical processes of the body may suffice to induce the clinical manifestations which are widely known as

epilepsy. The successful treatment of the epileptic patient must, therefore, necessarily be individual rather than general, and be directed firstly to eliminating as far as possible the factors which tend to precipitate or aggravate the condition, and, secondly, to improving the stability of the nervous system.

Etiology. *Heredity.*—Evidence of the direct inheritance of epilepsy is relatively uncommon, occurring only in from 10 to 20 per cent. of the cases. A neuropathic heredity, on the other hand—insanity, alcoholism and definite neuroses in the forbears—is present in probably over 65 per cent. of all cases of idiopathic epilepsy. This is not surprising if we regard epilepsy as a state of instability rather than as a disease, for it is only natural that such a condition should result more commonly from an inherited neuropathic tendency than from the direct transmission of an identical state.

Sex.—Idiopathic epilepsy occurs rather more frequently in females than in males.

Age.—The great majority of cases begin in childhood, or at puberty, few cases arising after the age of thirty.

Syphilis.—Syphilis is undoubtedly a cause of organic epilepsy, but there is no evidence to point to its being a frequent factor in the production of the idiopathic disease.

Infective Fevers.—The disease occurs in children in association with the acute specific fevers, and it is possible that toxins play a part in starting the epileptic habit.

Trauma.—Trauma is a common cause of the organic form, but it is not infrequently apparently responsible for the development of the idiopathic form.

Reflex Factors.—Dentition, diseases of the nose, throat and ear, errors of refraction, alimentary disturbances, intestinal worms, circulatory disturbances, menstruation and emotional shocks are all responsible as reflex factors for the production of the disease.

Treatment. *Prophylaxis.*—From what has been said above it will be obvious that a neuropathic heredity is the most common cause of epilepsy, and that if the disease is to be lessened, intermarriage between those who suffer from neuropathic conditions must be discouraged. So far it is not possible to prevent such marriages, and it will only be by educating the public to realise the dangers of such unions that any material steps can be taken towards this end. As physicians it is our duty to dissuade neuropathics and epileptics from marriage.

The offspring of such marriages must always be treated as potential epileptics, and their upbringing, education, mode of life and general hygiene so ordered as to minimise the natural tendency to develop the epileptic state. A history of teething, convulsions and faints should be taken as a danger signal in such cases.

Attention to possible reflex sources of irritation must be regarded as a prophylactic measure in those with the epileptic tendency, and just as important on the preventive side in the early stages as on the curative in the later.

General Management and Treatment.—Before deciding upon the mode of life and the line of treatment to be advised in any case of epilepsy, three factors must be taken into consideration. (1) The social and economic position of the patient. (2) The type of epileptic. (3) The character of the disease.

1. *Social and Economic Position.*—If the patient's social and economic position is not such as to ensure the provision of adequate treatment in proper surroundings at home or in private, it is best to place him in an institution. In epileptic colonies or private institutions provision can be made for the education of the patient, supervision as to feeding and exercise, and the enforcement of a regular routine life in the circumstances best suited to his state. Occupation is provided of a kind which will not expose the patient to undue risk of injury in the event of his having a seizure, and in most cases it will provide him with out-of-door work. In such an institution the requisite control can be exercised, and there can be no doubt that a healthy routine life can be provided for patients who otherwise could not afford the expense which would be incurred in carrying out such treatment at home.

2. *The Type of Epileptic.*—The severer grades of epilepsy with mental defect, or the degenerate type of epileptic, cannot be dealt with at home, and their condition requires that they be placed in some suitable institution. Certain cases will be best treated in asylums, but less severe ones may do well in "colonies" or similar private institutions. If, on the other hand, the mental state of the epileptic is good, and the frequency and severity of the attacks are not extreme, and many epileptics are intelligent, artistic and intellectual, and quite capable of taking an active part in life—treatment at home or in the country can usually be carried out successfully, and the patient enabled to earn his living or pursue some occupation. Such cases make good patients, they realise the importance of a regular life, submit to the necessary limitations, and are eager to continue medicinal treatment. They therefore should not be placed in institutions, but, rather, encouraged to make the best of life and their opportunities.

3. *Character of the Disease.*—This factor is distinct from the previous one, though nearly connected with it. In dealing with the character of the disease one has to take into consideration: (1) the mental state of the patient,

(2) the type of seizures—Grand mal, Petit mal—or combined, (3) the frequency of the attacks, and (4) the time of their occurrence. It is largely upon a study of these points that the question of medicinal treatment will be decided, not only as to the nature of the drug to be employed, but also the dosage and the time and frequency of its administration. This point will be dealt with further in speaking of medicinal treatment.

General Hygiene. *Childhood.*—Too much stress cannot be laid upon the necessity for insuring a firm but kindly discipline and control in the upbringing of epileptic children. They must be given plenty of exercise in the open air and must have regular times for getting up, taking their meals, and going to bed. They should have plenty of sleep in a well-ventilated room. The diet should be simple and nutritious, care being taken to prevent over-eating. Constipation is not uncommon, and has undoubtedly a bad effect on the disease. It can largely be avoided by training the child to go regularly to stool, but may require treatment by diet or medicine. Excitement and emotional disturbances must be reduced to a minimum, but this need not interfere with healthy enjoyment.

Education.—Some epileptic children are highly strung and fond of reading and lessons. In these cases care must be taken to restrict their study, and they must not be allowed to enter for any competitive examination. Other epileptic children are backward and averse from any learning and they require special instruction, and should be sent, if necessary, to special schools.

Prevention of Injury.—The danger of the child injuring himself in a fit must be guarded against as far as possible. He should not be allowed to sleep alone or to play in dangerous places, and the rooms in which he lives should be provided with fire-guards.

Adult Life.—Excitement must be avoided and emotional disturbance prevented as far as possible. The limitations to be enforced must depend on the individual circumstances of each case. Dances, theatres, music-hall performances, or even religious services, may have to be forbidden. Sexual excitement should be avoided and marriage is quite unjustifiable. The life should be routine and regular. Plenty of exercise in the open air is esential, and for this reason a quiet life in the country is preferable to one in town. When the patients' mental condition permits they should have intellectual as well as physical pursuits, and their occupations should not expose them to undue danger in the event of their having seizures.

Treatment of Reflex Factors. *Alimentary System.*—Reference has already been made to the importance of having regular meals, to the avoidance of over-eating, or of partaking of rich or stimulating foods, and it need hardly be added that alcohol should be forbidden.

Constipation not only upsets the patient's general health but may reflexly induce epileptic seizures and make the patient more liable to suffer from a bromide rash. That it may exist, despite the fact of the patient having a daily motion, is well known; care should be taken, therefore, to see that the intestinal tract is kept open. Having cleared the bowels well out, constipation can be prevented by the administration of petroleum twice or thrice a day, and, if necessary, of cascara or some other aperient at night time. A regular time for going to stool should be insisted upon.

Intestinal worms may be a reflex factor and increase the epileptic habit in children predisposed to the disease, or aggravate it in those who already suffer from it. Round or tape worms are more frequently an exciting cause than thread worms, but any such irritation must be removed.

Circulatory and Cardio-Vascular Systems.—Grave cardiac disease is rarely met with as a cause of epilepsy, but if it exists the exhaustion subsequent to major seizures may endanger the patient's life from cardiac failure.

Minor disturbances of circulation play a more important part in determining the occurrence and time of onset of the seizures than is yet recognised. The association of feeble circulation, of spasmodic vascular constriction, of migraine and of cardio-vascular upset, with epilepsy, is seen in many cases. The state of the blood pressure has undoubtedly a considerable influence on the time of onset of the attacks, but this factor must be repeatedly investigated in each individual case before any definite conclusion can be arrived at. In practice stimulants may often be found beneficial in cases of nocturnal epilepsy.

Ocular Defects.—Obvious defects, or those which cause eye-strain and fatigue to the patient, should be remedied, although their removal has never in my experience caused an arrest of the attacks; as the wearing of glasses necessitates a certain amount of risk to the patient in the event of his having a fit, a strong framework should be provided.

Mouth, Ear, Nose and Throat.—Any obstruction or local disease in the mouth, ear, nose or throat should be attended to. The removal of polypi, adenoids and enlarged tonsils often exercises a beneficial effect.

Otorrhœa should always be attended to, but it is very important to make certain that the fits associated with such a condition are due to epilepsy, and not to secondary intracranial complications.

Urinary System.—Examination of the urine

may reveal the existence of kidney disease or of some abnormal metabolic state which should receive suitable attention.

Dietetic Treatment. *Diet in Epilepsy.*—In general the diet should be simple but nourishing, and over-eating must be guarded against. Alcohol should be forbidden. Special diets have been recommended in epilepsy, and they require mention as in some cases they prove beneficial.

1. *A Salt-free or salt-restricted diet* has been advocated on the ground that the exclusion of salt (chlorides) enables the physician to give smaller doses of the bromides and thereby to lessen the risk of bromism. Experience with salt-restricted diets has not, however, proved it to be of any special value, except in cases where the bromides are badly borne.

2. *A Purin-free or Purin-restricted Diet.*—Purin substances are constructed on a base C_5N_4, and are present in all forms of meat extracts and in both red and white meats, liver, sweetbreads, salmon, plaice, halibut, also, to a less extent, in tea, coffee, cocoa. Non-purin foods are milk, butter, cheese, eggs, sugar, rice, macaroni, tapioca, white bread, cabbage, lettuce, cauliflour, fruits, olive oil. Vegetables other than the above contain varying quantities of purin. The results of purin-free diet have been good in a small number of early cases, and in some associated with migraine, but in confirmed cases little benefit has been observed. In general, if no improvement is noted in three months, the diet need not be continued.

Medicinal Treatment. *The Bromides.*—The alkaline bromides are the most serviceable drugs in the treatment of epilepsy, but their effect varies considerably in different cases. In a few cases bromide appears to aggravate the condition, and in some it has no effect, but in the great majority it lessens the frequency and severity of the attacks, and in a small number it effects a cure. Bromide, if given at all, should be given in a systematic manner continuously in suitable doses and combined with other drugs. Potassium, sodium, ammonium and strontium bromide have all been tried extensively, and of these potassium and sodium are the best. Bromides are apt to upset the stomach, and strontium bromide, though more expensive, has no special advantage. Some authorities prefer employing the mixed bromides. Bromide is of most service in cases with major attacks, and in cases with major and minor attacks, but is sometimes useful in cases of petit mal. There can be no doubt that the effectiveness of bromide can be increased enormously by judicious combination with other drugs. The question of dosage will be dealt with later, but it may be stated here that if 30 gr. of bromide given thrice daily have no effect, then it is unlikely that larger doses will be of benefit. In general a dose of 15 to 20 gr. thrice daily will be found sufficient.

Symptoms of bromism only appear when the drug has been pushed too far, especially if constipation is present. They consist of mental confusion, drowsiness and stupor, with loss of memory and sexual desire and power, associated with ataxia, dilatation of the pupils and anæsthesia of the palate and pharynx. The breath becomes fœtid and gastric symptoms are troublesome. The complexion is muddy and the skin dark, covered with an acne rash and usually cold and clammy. The heart may be affected, its action becoming rapid and feeble, and the temperature may be sub-normal.

Bromipin or Brominol is a combination of bromine and sesame oil. It is only absorbed in the intestine, and has little tendency to cause gastric symptoms or a bromide rash. It can be given in capsules of two strengths, 1 dr. doses corresponding to $\frac{1}{6}$ or $\frac{1}{2}$ dr. of potassium bromide. It does not appear to be more efficacious than bromide, but is a useful substitute in cases where bromide is ill borne.

Ethylene Bromide.—This is a colourless liquid, the dose of which is 1 to 2 min. Oppenheim has recommended its use in epilepsy. He gives it in the form of an oily emulsion containing 5 per cent. of ethylene bromide, the dose being 10 to 30 min. thrice daily in sweetened or peppermint water.

Monobromate of Camphor is indicated in cases with much sexual excitement. It should be given in doses of 2 to 5 gr. three times a day.

Bromural, in doses of 5 to 10 gr., has a distinct hypnotic effect, and is sometimes useful in cases of nocturnal epilepsy, when the attacks occur during the early hours of sleep.

Belladonna.—This drug is most useful when given in combination with bromide, especially in cases of petit mal. It is well worth trying alone in cases of minor epilepsy or in those in which bromide has no effect. It is best given in the form of the tincture in doses of 3 to 7 min. Belladonna may also be given in pill form, $\frac{1}{6}$ to $\frac{1}{3}$ gr. of the extract being given night and morning, and gradually increased. Oppenheim advocates small doses of atropine, $\frac{1}{200}$ to $\frac{1}{125}$ gr., several times daily in cases in which bromide has failed.

Borax.—This drug, like belladonna, is best given in combination with bromide, and should be tried in cases of mixed epilepsy with impairment of memory. It has been given alone, but without any great success. The dose in combination with bromide is from 10 to 15 gr.; when given alone larger doses may be employed, but they are apt to cause diarrhœa.

Zinc.—Zinc oxide, in doses of 1 to 2 gr., may have a wonderful effect in cases troubled with impairment of memory. Larger doses,

3 to 5 gr., thrice daily may be given in individual cases, but the drug sometimes causes vomiting.

Arsenic.—Arsenic is undoubtedly of service in preventing the occurrence of the bromide rash, and is as a rule well tolerated, although it tends to darken the patient's skin. In addition to this action, however, it is of great service as a tonic for debilitated patients.

Strychnine and Nux Vomica.—These may be useful in combination with bromide in cases where tonic treatment is indicated, or where depression forms a marked feature of the case.

Digitalis and Strophanthus.—These may prove very useful in cases of nocturnal epilepsy where the onset of the attacks is determined by enfeeblement of the circulation.

Iron.—Iron is sometimes beneficial in cases of epilepsy, but in a large number of cases it appears to increase the frequency and severity of the attacks, and must, therefore, be given with great caution.

Indications for the Choice of Drugs and the Method of their Administration

In all cases of epilepsy a chart should be kept in which is recorded, as far as possible, the time of occurrence and nature of the attacks, and with this should be noted the mode of life which the patient is living and the medicinal treatment which he is receiving, as in many cases experience alone will enable one to find out the most beneficial line of treatment.

In cases of mixed epilepsy, where the attacks occur at various intervals and at no special times, the drugs should be given thrice daily, the dose of bromide varying from 10 to 20 gr., according to the severity of the case. Arsenic and belladonna may be given in combination with the bromide.

In cases of major epilepsy, bromide and arsenic should be tried.

In cases of minor epilepsy bromide, belladonna and borax should be employed, the dosage and administration being determined by the severity of each case.

In cases of nocturnal epilepsy a large dose of bromide, 20 to 30 gr., with strychnine, digitalis or strophanthus, should be given at bedtime, and a half dose given in the morning before getting up.

If the attacks are serial and periodic, a moderate single dose should be given in the intervals, and larger doses more frequently at the period when the attacks are expected.

Treatment of the Attacks

If the patient has any warning he should immediately seek out a place of safety and lie down. If the attack has begun he should be placed flat on his back, a pillow being placed beneath his head and all tight clothing should be loosened. The convulsive movements should not be controlled more than to prevent injury. Some patients tend to roll over, and if this be a constant feature in any case provision must be made to meet it, as the risk of suffocation is not inconsiderable. The patient is apt to bite his tongue during the stage of clonic convulsion, but this can be guarded against by inserting the handle of a tea-spoon covered with rubber tubing, or a wedge-shaped piece of cork, between the teeth. When the attack is over the patient should be allowed to remain quiet or be sent to bed. Generally he feels dull, heavy and sleepy after an attack, but in some cases excitement or automatism may follow, and this necessitates careful attention. The headache which occurs after a fit may be relieved by phenacetin or antipyrin.

Treatment of the Status Epilepticus

In this condition the patient has a succession of fits, and passes into a state of coma, consciousness not being regained between the attacks. The mortality from this condition is nearly 50 per cent., and patients rarely survive more than two attacks of status. The cause of death in these cases is found in hyperpyrexia, exhaustion and cardiac failure. If the patient shows signs of passing into a condition of status, such as the onset of serial attacks, large doses of bromide and chloral should be given. If these fail to arrest the fits, inhalations of chloroform should be given, followed by hypodermic injections of hydrobromide of hyoscine, $\frac{1}{100}$ to $\frac{1}{50}$ gr. Hypodermic injection of a 1 to 3 min. of a five per cent. solution of hydrobromide of conine has been advocated for checking the convulsions and inducing sleep. If hyperpyrexia develops the patient should be treated in a continuous bath, or with cold packs to reduce the temperature. Nasal feeding may be necessary and cardiac stimulants may be required in order to keep up the patient's strength and to prevent cardiac failure.

Surgical Treatment of Epilepsy

In many cases the fits are attributed to some injury to the head which has occurred usually many months or years previous to the onset of the attacks, and the parents are often anxious to have the patient operated upon. In general it may be stated that, if the fits have no constant seat of onset or if there is no evidence of injury to the skull, operation should not be performed. Should, however, there be evidence of injury, and the seat of injury correspond to the cortical area in which the epileptic discharge originates, exploratory operation may be advised. In some few cases the removal of a depressed piece of bone or of scar tissue may result in a permanent cure. Operation is often followed by a period of relief from the attacks, extending for

about six to twelve months, but after that time the fits begin to recur as frequently as before. In the majority of cases no improvement at all is noted, and it cannot be said that surgical treatment has been followed by any considerable degree of success, even in apparently suitable cases. In all cases medicinal and general treatment should be combined with the surgical.

T. G. S.

HEADACHE

Headache is one of the most common symptoms which the physician is called upon to treat. It varies greatly in its character, and may arise from an almost infinite number of different causes. In order that treatment may be successful a correct diagnosis of the cause must be made in each case, and that will depend upon the skill of the physician and the thoroughness of his examination.

In diagnosing the cause of a symptom common to so many different diseases and conditions a process of exclusion must be employed, as otherwise grave mistakes are certain to be made. There is a tendency for specialists to attribute headache to diseases or abnormal conditions found in the special department of medicine or surgery in which they practise, without due consideration of the case as a whole.

Headaches may occur—

1. As a result of local disease of the skull, brain or membranes—tumour, abscess, inflammation, syphilis.
2. As a symptom in many general diseases—most acute febrile conditions, renal disease, gout, arterio-sclerosis, etc.
3. As a result of local conditions in the nose and accessory sinuses—eye (astigmatism, etc.), ear and mouth.
4. In various blood states—anæmia.
5. As the result of vasomotor disturbances which affect the intracranial blood pressure. They may be due to changes in the atmosphere, excessive normal reaction—as after hard mental work, or to auto-intoxications from various known and unknown causes.
6. In venous hyperæmia from chronic cardiac disease, emphysema, coughing, violent strain or obstruction to the venous return in the neck.
7. In anæmia from posture, shock or aortic disease.
8. As a symptom of neurasthenia.

The treatment of headaches due to local disease of the brain, skull or membranes, or arising as a symptom in acute febrile or general diseases, should not be divorced from that of their causal conditions.

Migraine and Periodic Headache.—Under this heading is grouped a large number of cases in which the patients suffer from periodic or paroxysmal attacks of headache which are not associated with any definite organic disease or structural change.

Migraine, or hemicrania, is a very distinct and definite clinical entity, and it might be urged that it should be dealt with alone, but as it and the other forms of periodic headache have a common origin in a disturbance of the vasomotor mechanism they are better considered together, migraine being taken as the most typical example of this group.

Migraine affects both sexes; it may begin in childhood, but most commonly about the time of puberty. The attacks are paroxysmal in character and may recur at varying intervals, the tendency being for them to become less frequent as the patient grows older. The malady is often hereditary, but there is no evidence that it is specially associated with a neuropathic heredity. The immediate cause of the attacks is a spasmodic contraction of the cerebral arteries on one side of the head, with a subsequent dilatation of unusual degree which may persist for a long period. There is abundant evidence to show that in many cases the spasm may not be confined to the cerebral system, while in others it would seem that the spasm may be extremely local in extent.

The patient may be aware of an impending attack owing to a sensation of fullness in the head, or to sensations peculiar to each individual case; but in most instances a period of unusual well-being and mental alertness precedes the attack, and investigations of the blood pressure at such times show it to be raised. Some authors have described a period of unusual well-being after an attack, but this is exceptional, and as a rule, especially if the attack has been severe, the patient feels weak and irritable and disinclined for any exertion.

Mode of Onset and Character of Attack.—A fully developed attack of migraine is characterised first by a stage of chilliness and pallor, the vision becomes affected, objects appear blurred or the patient complains of being unable to see in front of him or to one side, owing to the development of central scotoma or hemianopia, with which is associated numbness and paræsthesia. If the hemianopia is on the right side in a right-handed person, paraphasia and mental confusion may be present; in some cases the patient is conscious of a metallic taste in the mouth. Frequently bright, scintillating lights appear, either in front of the patient or in the hemianopic field, in which case they may assume the typical fortification appearance. After lasting for from five minutes to half an hour these symptoms begin to pass off and are replaced by a dull, boring pain, generally confined to one side of the head (that opposite the side of the hemianopia), and situated usually above the eye or in the temple region. The

pallor disappears and the patient experiences a sensation of warmth, his headache increases in severity and every pulse-beat becomes an agony. Movement of the head, bright light or noise increase the pain, which may be most severe and prostrating and accompanied by vomiting. The duration of the headache varies from half an hour to forty-eight or fifty-six hours according to the severity of the attack, and it may be three or four days before the patient feels restored to his normal condition. In most cases the patient passes a large quantity of pale urine when the attack is passing off. Those who are victims of migraine may only occasionally suffer from severe attacks, but are subject to minor sensations in which, as a rule, there is chilliness succeeded by unilateral headache. In addition to these there are many more who suffer from hemicrania, which in all particulars is identical with the minor attacks occurring in true migraine.

The Causation of the Vasomotor Disturbance.—The cause of the vasomotor disturbance is not fully understood; it may arise from such various conditions as shock, exposure to cold, or intoxication from the gastro-intestinal tract. Certain by-products of disordered intestinal digestion are well known to have a powerful action on the vasomotor system, and this probably constitutes the commonest cause of migraine. Further, in a small number of cases individual idiosyncrasies in regard to protein metabolism account for this condition.

Exciting Causes.—The onset of an attack in those predisposed to the condition may be determined by many causes. Most important of all is fatigue, often brought on by going too long without food, or by overwork—physical or mental. Worry, excitement, working in a vitiated atmosphere, travelling in a vibrating conveyance, looking at moving pictures or small-check patterns, smoking on an empty stomach or indiscretions of diet. In women attacks are specially liable to occur at the times of the menstrual periods.

Preventive Treatment.—From what has been said above it is obvious that attention to general hygiene, the avoidance of exciting causes, and the maintenance of general health are essential if any success is to be obtained in alleviating the condition. All errors of refraction should be corrected. If the patient's occupation be sedentary he must be made to take regular exercise in the open air, but not permitted to overtire himself. The state of the alimentary system requires special consideration.

Treatment of the Attacks.—Very little can be done to cut short an attack once it has fully developed, but if taken at the onset of the chilly stage it may often be aborted. As soon as the patient realises that an attack is beginning he should take a large dose of one of the following remedies—

Phenacetin, 10–15 gr.
Phenazone, 10–15 gr.
Antifebrin, 1–3 gr.
Migranine (a mixture of antipyrine with caffeine and citric acid), 10–15 gr.
Aspirin, 15–20 gr.
Pyramidon, 5 gr.

Experience alone will show which of these is the most serviceable, as some patients are relieved by one more than by another. Phenacetin, in 10 to 15 gr., combined with 5 gr. of caffeine, is perhaps the most universally successful. These drugs are best given in the form of a powder, and their action may be promoted by taking a glass of hot water, or half an ounce of brandy in a little water. Some authorities recommend larger doses than those given above, but the results do not warrant the risk attendant upon them.

Having done this, the patient should rest quietly in a well-ventilated room, and, if he feels chilled, should place a hot-water bottle to his feet and hands. He will know that the attack has been warded off if, when the feeling of chill has passed, he is free from headache.

If the attack be fully developed the patient should lie on his bed in a darkened room, or sit in an armchair—some experiencing less pain when in an upright position. Hot-water bottles applied to the feet and the back of the neck are comforting to most people. A small dose of—

Phenacetin, 5 gr.
Caffeine, 1 gr.

should be given, and this can be combined with a drachm of Easton's Syrup, or with bromide and strychnine. If vomiting occurs, brandy should be administered. If the attack be very severe the patient should go to bed and endeavour to sleep it off, and for this purpose he should be given a dose of bromide and chloral, or 7 gr. of veronal, but these drugs should always be administered by the physician, and not left to the discretion of the patient. A local application of menthol is very soothing and is often successful in inducing sleep.

Medicinal Treatment between the Attacks.—Gouty people should be given a blue pill and a dose of Carlsbad salts once a week as a routine remedy.

Anæmic and ill-nourished patients require general tonic treatment, and always benefit by taking suitable preparations of iron and arsenic.

Neurotic patients may require tonic treatment, but of all drugs bromide, combined with strychnine or with nux vomica and arsenic, will give the most relief.

In cases with continuous high blood pressure iodide or nitroglycerine, in the form of Liquor

Trinitrini, may be given, but should not be used continuously, as they tend to lose their effect. T. G. S.

NEURASTHENIA

Introduction.—Before discussing the treatment of neurasthenia it is necessary to define what is meant by the term, for although most medical men understand what is implied by it, yet it has been applied very loosely to include conditions which are entirely distinct from it, such as hysteria and various forms of insanity. Some authorities have sought to limit its use by defining it as a primary fatigue neurosis, but in practice such a definition is too restricted and would exclude many perfectly typical cases. There is no doubt that many grave physical and mental diseases give rise to symptoms identical with those of neurasthenia, but careful observation and examination should enable one to recognise the true nature of the case.

For the purpose of this article neurasthenia is defined as a mental and physical state characterised by a combination of symptoms, some objective and others subjective, arising in association with many different conditions, mental and physical, but independent of any recognisable organic lesion of the nervous system.

It is not justifiable in the present state of our knowledge to consider neurasthenia as a disease, although it is a definite clinical entity. The different ways in which it may originate, the variations in its manifestations, and the totally different methods of treatment which may result in its cure all point to its being a state of mind and body rather than a definite disease. It can never be held as being purely physical, nor on the other hand as purely mental.

Etiology.—A neurasthenic tendency may be inherited. This is seen not only in families but also in certain races. These people may not normally suffer from neurasthenia, but are liable to develop it with undue facility.

As direct causes—overwork and worry, long-continued emotional strain and stress, shock or extreme physical exhaustion are the most common. Ill health, gastric disturbances, constipation colitis, anæmia, uterine or ovarian troubles, excessive sexual intercourse or self abuse may all, by inducing a state of debility and exhaustion, give rise to symptoms which may later develop into neurasthenia.

Classification of Neurasthenia.—It is only natural that such a condition with so many and varied manifestations should be classified by different writers into separate types. The majority have divided the cases of neurasthenia into cerebral, spinal or cerebro-spinal types, according to the predominance of the various symptoms. From the point of view of treatment, however, it is better to classify the types by determining as far as possible the exciting cause in each case. This may only be discovered by a prolonged and careful investigation, which is necessary not only to find out the cause of the neurasthenia and so exclude the presence of grave but undetected organic disease, but also to give the patient that confidence in his doctor without which all treatment will fail.

The examination will reveal some cases as arising primarily from (1) physical exhaustion, disease, or disorder of function; (2) mental exhaustion and worry and anxiety; (3) trauma, with or without physical injury. Although neurasthenia may develop as a result of any of the above causes the patient does not suffer from neurasthenia until an element of doubt, fear or anxiety becomes added to the original symptoms. The man who suffers from some physical disorder or exhaustion may complain of fatigue, loss of brain power, pain, etc., without becoming neurasthenic. Similarly, in cases of overwork a man may experience a feeling of fullness and pressure in the head, may be conscious that he cannot work as well as formerly, that work requires more effort, and that his powers of concentration are failing, and yet not be neurasthenic. In traumatic cases hysterical symptoms may arise at the time of the injury, but neurasthenia rarely develops within three to six weeks after the injury. In all these cases the symptoms present may be those which are typical of neurasthenia, but it is only when the element of doubt begins to fix itself in the patient's mind that he becomes a victim of neurasthenia: fear that he may lose his health, that he will not recover, that his mind is giving way. Such apprehensions may be at first almost unconscious, later more insistent, and as a rule the patient keeps them to himself until obliged to seek relief by telling his doctor or his friends.

Symptoms of Neurasthenia.—The symptoms of neurasthenia vary in their type according to the intellectual status of the patient. In brain workers they are referred chiefly to the mind—mental fatigue and lassitude, loss of nerve power and concentration, indecision attended sooner or later by a vague unhappiness deepening into depression associated with attempt at self deception and subsequent remorse. To these are added pains, feeling of fullness and congestion in the head especially on mental effort, anxiety about the future, the possibility of continued ill health, inability to work, or the fear of approaching insanity. Alive to the necessity for effort yet unable to make it, the patient's mind becomes filled with a whirl of worry, doubts and fears, which prevent his seeing any way out of his difficulties, render him hopeless and unable to think clearly or to

sleep. In others of a more phlegmatic temperament the lack of effort and loss of will power are not accompanied by acute worry or fear, and they become reconciled to an invalid's life, absolutely self-centred, posing as martyrs bravely suffering, and yet living a life of self, able only to do what they desire to do and wearing down their best friends by a truly colossal obstinacy and passive resistance. Those whose work is mainly physical suffer from loss of will power and lassitude, but this does not cause mental worry, and their chief complaint is of pains and aches referred to the body or limbs which prevents them from carrying on their work.

Another factor which plays an important part in determining the nature and situation of the symptoms in any given case is the presence of any physical disorder or defect; for example, in cases with alimentary disorders—gastric and intestinal symptoms may predominate, or in cases with astigmatism—pain referred to the eye and head.

Treatment of Neurasthenia.—From what has been said above it will be obvious that the first essential for success is to gain the confidence of the patient. To do this the physician must listen patiently and attentively to the patient's recital of his ills and symptoms, encouraging him by judicious and pertinent inquiries to make his statement more clear. This must be followed by a careful and exhaustive examination into his physical condition in order to exclude the presence of incipient, grave, but undetected organic disease, or to discover any slight physical disorder which might be responsible for the symptoms. By these means it may be possible to find out the cause of the patient's trouble, which he has, perhaps, not directly revealed, but which he is relieved to have explained to him. Being certain that there is no serious organic mischief, the physician can then assure his patient that he is not suffering from any serious or incurable complaint and that he will not lose his reason. Further, he must explain to him how the symptoms arise and that with appropriate treatment they will disappear, and reassure him as to the future. Such an explanation will only be possible or acceptable if the examination of the patient has been as complete as even he desires. The general practitioner has often to deal with neurasthenia in its early stages when it may be impossible to tell whether the symptoms are indicative of some grave disorder or not. In such instances he may not have decided in his own mind as to the nature of the case, and few people possess the gift of dissembling their doubts from an anxious patient. For this reason a second opinion is often advisable, as the consultant has the advantage when he sees the patient of having the case laid before him by the patient's doctor and the opportunity of making a prolonged and careful examination, and finally of expressing an opinion which the patient is more or less prepared to accept with confidence.

Slighter Cases of Neurasthenia.—These may be completely cured by careful examination and the judicious explanation of the symptoms to the patient, which will give him the reassurance he requires and dispel the fears which have aggravated his condition. At the same time appropriate treatment must be prescribed for any disorder of function or physical ailment which may have been discovered. If necessary, a holiday should be advised, either with exercise or leisurely travel with suitable companionship, according to the physical and mental state of the patient.

Severe Cases of Neurasthenia.—In these, further and more extended treatment may be necessary, and the requirements of each case must be considered individually. The method most commonly adopted is that of the rest cure, which will always be associated with the name of Weir-Mitchell.

Rest Cure.—Before beginning a rest cure the patient must consent willingly to undergo whatever treatment is considered necessary. The strictness of the rest cure and its duration will depend upon the nature of each individual case. It is most important to insist that once it has been entered upon it is carried out along the lines laid down.

The patient is separated from all friends and relatives, and in order to remove him from associations which militate against the cure he should be placed in a nursing home.

It is almost impossible to carry out a rest cure at home, and to attempt to do so is undesirable except in cases of pure physical exhaustion.

The nursing home should be quiet, and for this reason surgical homes should be avoided. The room should be fairly large, cheery and well ventilated. Coke or gas stoves should not be allowed, as they tend to make the air too dry and reduce the vitality of the patient. The nurses must be experienced in the management of such cases, and must be quiet, well-trained, patient, attentive, kind, sympathetic but unemotional, and with plenty of tact and firmness. The food should be well cooked and daintily served.

In a rigid rest cure the patient is isolated and cut off from all communication with friends or relatives. Reading, writing or working are forbidden. Absolute rest in bed is insisted upon, and to begin with only milk or milk and rusks are given to the patient. The patient is fed every two hours, four ounces of milk being given at a time; this is rapidly increased until the patient is taking eight to ten pints of milk

in the twenty-four hours. After two or three days a small morning meal may be given, and later a mid-day or evening meal, the amount of milk taken being reduced. Fish, bacon, eggs, cutlets, green vegetables, milk puddings, bread, butter and cream may be added to the dietary.

The bowels must be kept regular, which may be no easy task with such diet, but an occasional dose of calomel and salts, senna pods, or cascara, along with pure liquid paraffin once or twice daily will usually prove effective even in cases of chronic constipation, more especially if the patient is given abdominal massage every day.

In order to keep up the tone of the patient and to compensate for lack of exercise abdominal massage should be given twice daily morning and night. At first it should be gentle and restricted to fifteen or twenty minutes at a time, but as time goes on it may be given more vigorously for a longer period. After the massage the patient should be encouraged to sleep and at night time the massage should terminate with gentle massage of the head and face. If the patient does not sleep after massage it should not be given at night time. During the second week the massage may be supplemented by mild general faradism, sufficient to cause a slight contraction of the muscles.

The duration of the rest cure should be from six to ten weeks, the restrictions becoming less severe as the patient improves, and resistance exercises being added to the massage. Before leaving the home the patient must be gradually allowed to sit up in the room, go out for drives and later to walk in the open air. The patient should not immediately return to work.

A strict Weir-Mitchell cure is applicable to very few cases. It is most serviceable in cases of physical exhaustion, especially those dependent on malnutrition or starvation—anorexia nervosa. Modified rest cures are indicated in all cases of physical fatigue or overwork, modified especially as regards diet and baths and with less restriction as to reading, work, knitting, sewing, etc. and games. The inadvisability of permitting writing or visitors in cases which are suitable for rest cure treatment is obvious.

Many cases of neurasthenia are not suitable subjects for rest cure treatment. Those in which there is no physical exhaustion, but simply lack of circulation, require rather routine treatment and exercise, preferable in the open air, and this is best carried out in some home in the country where due supervision can be obtained along with the opportunities for outdoor exercise and occupation. Another type of neurasthenia which should not be placed in a home for rest cure is that in which depression is mental. These cases are best treated by finding for them occupations and interests outside themselves, either in exercises or games, or in change and travel with a suitable companion, at the same time not neglecting to treat any physical trouble which may aggravate their condition.

Traumatic Neurasthenia.—The symptoms of traumatic neurasthenia rarely manifest themselves until two or three weeks after the injury. Their onset is often insidious and frequently escapes attention.

Those who have been exposed to severe shock, even if the physical injury be not great, should be made to rest quietly for some days, and if careful examination has failed to detect any serious damage they should be definitely reassured on the point. If symptoms appear a rigid rest cure should be imposed, followed by a period of change and occupation. In the case of the working classes this line of treatment is rarely possible. The circumstances attending such cases are particularly favourable to the development of neurasthenia. The patient, usually a member of a sick club, knocks off work and goes on the club. He may attend some hospital or private doctor and receive a bottle of medicine or liniment; but beyond this nothing is done for him, and he spends his day loafing about and often smoking and drinking too much. He may brood over his symptoms or may pass into a state in which he prefers to live on half pay doing nothing rather than making a genuine effort at resuming his occupation. If he comes under The Workmen's Compensation Act and is in receipt of half wages and sickness benefit he may receive sufficient money to enable him to exist without working. If legal proceedings are taken he is subjected to medical examinations—is forced to retail his symptoms, and his condition is aggravated by the worry and uncertainty about the future proceedings. Many men are deterred from resuming work simply because they feel that if they secure work they will have forfeited their compensation, should they subsequently find themselves unable to carry on their occupation. Until adequate provision is made for the prompt treatment of such cases these difficulties will continue in many cases to be insuperable.

Sexual Neurasthenia.—This form of neurasthenia is most obstinate and peculiarly depressing to the patient. It may arise from different causes and its treatment must be directed accordingly. It may originate (1) from general debility and failing sexual power, (2) from exhaustion due to excessive sexual intercourse or self abuse, (3) from the mental effect of previous venereal disease or self-abuse. These are associated in the patient's mind with his symptoms, which may really depend on general debility or overwork.

Electrical Treatment.—Faradic electricity may be considered as a useful adjunct to the massage, but if it tends to excite the patient it should not be persisted with. In cases requiring stimulation it will be found to be most effective. High frequency is also of great service in many instances.

Hydrotherapy.—Hydrotherapy may prove a useful adjunct to the rest cure or home treatment of neurasthenia. The pack, hot or cold, and warm baths are often useful when insomnia and restlessness are outstanding features. The spinal douche is of most service in cases of sexual or traumatic neurasthenia where the patient requires stimulating. In some cases where the patient is nervous an ether or ethyl chloride spray may be substituted for the spinal douche.

Suggestion.—Suggestion may prove helpful in cases which are complicated by "phobias," but hypnotism is not suitable to the majority of cases. Persuasion and re-education are of undoubted value in some cases.

Psycho-analysis.—It is difficult at present to speak definitely of this method of treatment. It is not necessary in the majority of cases, but its value in selected cases cannot be denied.

Drugs.—The question of drug treatment must be decided by the physical and mental state of the patient. Of tonics, arsenic is the best, and nux vomica and iron are often serviceable. Strychnine is useful in some cases but contra-indicated in many.

Bromide and valerian are the most helpful drugs where sedative treatment is necessary. For the treatment of insomnia the reader is referred to the special article on that subject.

Organo-therapy.—Many preparations have been prepared and placed on the market. Of these spermin is probably the oldest. That they may occasionally do good cannot be denied, but that they succeed apart from other forms of treatment is very doubtful.

After-treatment of Neurasthenia.—Not less important from the point of view of the patient is the after-treatment, and this must depend upon the necessary adjustment of the patient's habits and mode of life to suit the requirements of his physical and mental state. Such advice coming from some one whom the patient regards as understanding his case will be duly followed and may prevent any recurrence of the neurasthenia.

T. G. S.

HYSTERIA

Hysteria is due to disordered function chiefly of those elements of the nervous system which are concerned with psychic processes. A nervous system unstable as the result of neuropathic heredity is the usual seat of the disease and an upbringing throughout childhood and early adult life the least calculated to produce vigorous mental and physical health with a sound and cheerful outlook upon the future, is frequently a fostering cause. The subjectivity of mind and the love of sympathy engendered by feeble physical health and the difficulties of attaining a comfortable mental perspective upon matters of sex and religion are common antecedents, while mental and physical shocks of any kind, strain and grief are usual immediate exciting causes for the appearance of symptoms. It follows therefore that the treatment of hysteria, both preventive and curative, must consist (1) in the removal as far as possible of exciting causes, (2) in measures calculated to influence the mental state, amongst which the personal influence of the doctor and of the nurses, impressive treatment such as electricity, the rest cure, hydrotherapy, psychoanalysis and hypnotism may be mentioned in that order of importance, and (3) careful attention to the condition of nutrition and to general health.

In the treatment of every case of hysteria there are three points that must be especially borne in mind :—(1) There is no routine treatment for the malady, but every patient must be treated individually according to the causation of the trouble, its symptoms, and according to her personality. For example, to order isolation to a patient who has recently broken down with acute grief—to shut her up with her grief, in fact—would be a measure both useless and lacking in common sense, whereas in the naughty spoilt hysteric of the sympathy-demanding type, isolation would be indispensable. (2) In so far as hysteria is of recent onset, and especially if there is a definite exciting cause for the appearance of symptoms, it is a readily curable condition, but speaking generally the more longstanding the symptoms and the greater the number of times that the patient has broken down, the worse the prognosis. Severe and long-standing hysteria is often the most incurable of diseases, and it may even prove fatal from inanition. For habit may impress the nerve elements just as indelibly as it may impress the individual and to an extent that no training will delete, and when nerve elements have remained in an unvarying condition of disordered function for years a return to normal function is unlikely.

(3) Certain organic diseases of the nervous system may in their early stages present a symptom-complex indistinguishable from that of hysteria, and further, organic nervous disease and hysteria may be coincident. Disseminate Sclerosis and Subacute Combined Degeneration are the maladies especially important in this connection. The treatment for hysteria often removes the symptoms in these cases, in which an erroneous prognosis is sometimes inevitable.

A frequent and careful search for the signs of organic disease on the one hand and for definite hysterical stigmata on the other is essential. Sometimes the absence of improvement under treatment in an apparently favourable case simulating hysteria will suggest to the medical attendant that he is in reality dealing with a case of organic nervous disease.

The preventive treatment of hysteria is concerned with children of neuropathic heredity or of families in which other members have suffered, and with the after treatment of those patients who have recovered from hysteria. In childhood careful hygienic principles and a robust mental and physical education with an absence of all coddling, valetudinarianism and undue sympathy and early and kindly instruction upon matters of religion and sex are important. Neurotic parents are the worst association for neurotic children, and the early removal of the child from home influence to a good school is often as advantageous as it is difficult to bring about. Those who are recovered from hysteria should if possible change their surroundings, adopt the most healthful routine of life and above all acquire a definite aim and object in life.

The question of marriage in the subjects of hysteria is an important one, but no definite rule can be laid down. That hysterical manifestations ever have their origin in unsatisfied sex feelings or that marital relations have any beneficial influence upon hysteria is open to the gravest doubt, and it cannot be disputed that marriage and the strain of household duties and motherhood are sometimes the cause of grave and intractable hysteria. Yet it is not infrequently found that marriage benefits the hysterical subject, conceivably by increasing the interest and aim of life.

It is all essential in the first place that the complete confidence of the patient shall be gained so that the medical attendant may investigate, comfort and advise upon any matters of grief and worry that may be causing the disease. It is always advantageous to remove the patient from her usual surroundings to a nursing institution or to the care of friends, or to place her in charge of a responsible nurse who is skilled in the care of hysterical patients.

The personal influence of the medical attendant upon his patient cannot be over-estimated in the treatment of hysteria, and inasmuch as he can inspire her with his complete knowledge of her illness and his ability to cure it, and in proportion as he can dominate her personality, his success will be assured. He must show his patient that he is convinced of the reality of the disease and of its speedy curability; and since the term hysteria is associated in the lay mind with shamming and mental weakness, he should avoid the resentment which the use of this word may arouse in the patient and her friends by referring always to the malady as "functional nervous disease." His attitude must be kindly, firm, and confident, and he must never show himself taken aback by any development of symptoms or failure of treatment. He should see his patient often and be impressive in the arrangement of the details of treatment and must steer a judicious course between over-attention and neglect, between cajolery and bullying, and between sympathy and teasing, always bearing in mind that punitive measures both in words and in treatment rarely do good and often do much harm in the treatment of hysteria. It sometimes happens that all the efforts of the medical attendant are met with resentment and dislike on the part of the patient, and in such circumstances it is best to place the patient at once in other hands. The nurses selected for the care of hysterical patients should if possible be those who have had special training in nervous diseases and should be of tactful, cheery and masterful dispositions.

Electrical treatment is often of great benefit in conditions of hysterical paralysis, contracture, blindness and sensory loss. Sometimes a single application will remove all the symptoms, more commonly a slow improvement takes place. It is probable that the effect of the electricity is entirely a psychic one and should therefore be applied with due ceremony. Faradism, the static breeze and high-frequency currents may be employed indifferently or may be alternated from time to time. Great care must be taken that the patient is not frightened or hurt, and strong currents should only be used upon regions which are insensitive. With nervous patients it is better to commence electrical treatment with Faradic massage—a gentle current being applied through the hands of the nurse. In hysterical aphonia Faradism may be applied with the hand to the front of the neck or by means of a small electrode to the fauces. General mild Faradism is often useful in any case of hysteria.

Massage is generally beneficial. It improves the nutritional state and impresses the patient that something active is being done for her cure and the same holds good for spinal douches, electric baths and sulphur baths, the latter especially being a safe and impressive remedy. It must not be forgotten that some patients have a natural objection to being touched, and when this is the case it is well not to enforce massage as no benefit is likely to be gained thereby.

Hysterical paralysis, contractures and aphonia may be sometimes removed by the following simple means: The patient is placed lightly under the influence of ether until the noisy

struggling stage of the anæsthesia is reached when she is likely both to use her larynx and to struggle with the hitherto useless limbs. The anæsthetic is at once discontinued when this result has happened, and as she regains full consciousness her attention is forcibly directed to the fact that her limbs are moving or that she is using her voice or that the contracture has disappeared as the case may be.

Weir Mitchell Treatment is best employed for the more chronic cases and where a poor nutritive bodily state seems a contributory cause of the nervous derangement and where there is no mental distress that isolation might increase. Thus deprived of any exciting causes that may be keeping up the functional derangement, the patient is in the best position to profit by any treatment of body and mind that may appear advisable. The length of this treatment and the degree of the isolation will of course be determined by the individual case. As the patient improves the stringency of the treatment may be relaxed and amusements allowed, and at the conclusion of the treatment a pleasurable holiday with a capable companion is always a necessity before returning to ordinary life. It cannot be too strongly insisted that the success of a "rest cure" in the treatment of hysteria depends upon the relations of the physician and the nurse towards an impressionable patient and that the selection of a nurse skilled and successful in the treatment of such cases is absolutely essential.

Psycho-analysis has originated from Breuer and Freud of Vienna, who consider that the symptoms of hysteria are due to some mental experience the unpleasant memories of which have become dissociated from the conscious mind and repressed into that of the subconscious. But though outside of consciousness, the memory is still there and is capable of influencing the feelings and the actions of the patient without his recognition. The method of treatment consists in encouraging the patient to communicate his ideas as they occur to him with complete freedom, no matter what their nature. From this free association of ideas the physician picks out the salient points and weaving them together gradually arrives at the buried memories of the subconscious mind, which thus brought out become part of the patient's conscious mind and are then associated normally with other thoughts. By restoring these reminiscences to their proportionate place in the mental surroundings they cease to act independently and are no longer a source of trouble. This treatment can only be carried out by an expert in the method and its advantage over other methods in the treatment of the less severe cases of hysteria has not yet been conclusively shown. Yet in patients who have resisted other modes of treatment it should certainly be given a trial.

Hypnotism has been recorded as successful in some cases, but it has not infrequently aggravated the condition of others, and it is so often a complete failure that its employment is to be deprecated except as a last resort where all other means have failed.

Whatever line of treatment is adopted it must be recognised as early as possible whether the patient is improving or not, and if no improvement is being made it is better to make a radical change in the treatment. The methods which have cured a patient upon one occasion are very likely to fail upon a second occasion, since she has become conversant with the treatment and is less likely to be impressed by it. Therefore in treating patients who have relapsed it is wise to adopt different measures from those which have been formerly employed, the exception being when the patient shows unbounded faith in those measures which cured her in the first place.

The treatment of the general health of the hysterical patient is often of great importance. The condition of nutrition should be improved by careful feeding and tonics, fresh air and a strictly hygienic mode of living. Any condition of anæmia must be combated. Gastro-intestinal disorders are very common in association with hysteria both as cause and effect and must be thoroughly dealt with. Indeed it is probable that the value of the remedies long used in this disease—valerian and asafœtida, is due to their action as carminatives and in relieving enteric spasm. Great benefit is often attained by the use of certain calmative drugs which tend to decrease the subjectivity of the patient and lessen her reaction to irritating influence, and which induce restfulness, and increase the feeling of well-being. Of these Sodium Bromide in ten-grain doses thrice daily, conveniently combined either with Strychnine, Arsenic and Glycerophosphates or with an alkaline carminative, is indispensable. Aspirin in ten-grain doses thrice daily is also a valuable remedy, acting as a calmative of the nervous system and as an intestinal antiseptic. In cases where restlessness is a marked feature both of the preceding drugs may be given with advantage.

Hysterical fits are best treated at the time by a strong sensory stimulus such as dashing cold water over the face and neck, pressing upon the supra-orbital nerves, or best of all by applying the wire brush of a Faradic machine to the region of the nose. This is the only symptom of hysteria for which punitive treatment is admissible, the result being generally the immediate cessation of the fit. Otherwise hysterical attacks are best treated by neglect.

True hysterical attacks do not often occur without an audience, and the greater the consternation produced among the audience the more violent the attack becomes. The more the patient is held down to prevent her doing damage the more she struggles. Unresisted and in the absence of any audience to be impressed or to sympathise the hysterical attack soon ceases. Where hysterical fits tend to occur at the menstrual times a few doses of Bromide and Chloral are often of signal benefit. The great difficulty in dealing with all cases of functional fits is the making sure that they are not post-epileptic manifestations following slight and momentary attacks of minor epilepsy. The history must be carefully gone into for epileptic manifestations such as minor attacks, tongue-biting, enuresis, etc., and the commencement of the attack carefully scrutinised for evidence of "petit mal". It must be remembered that an hysterical attack does not suddenly occur without cause in an otherwise healthy person, and that such an attack occurring when the patient is asleep is perhaps always post epileptic.

J. C.

INSOMNIA

A thorough investigation of the causal factors is the first step that must be taken in the treatment of every case of sleeplessness. To help us in this investigation it is convenient to consider cases of insomnia as falling into two groups: (1) Extrinsic or symptomatic insomnia, in which sleep is interfered with by some condition of bodily discomfort such as pain, irritating sensations, pyrexia, dyspnœa, cough, cardiac unrest, gastro-intestinal ill-health, anæmia and starvation; and (2) intrinsic insomnia, in which no definite bodily cause can be found, and this group may be divided into three subgroups: (*a*) psychic, (*b*) toxic and (*c*) senile. This useful classification is, however, obviously an artificial one, for the true factors of insomnia must be an abnormal physiological state of the nerve elements produced either by their nutritional processes being defective, or from some toxic substance circulating in the blood, or from unusual peripheral stimulation. Often more than one of these factors is present, and when this is so a vicious circle is set up, since the lower the nutritional stability of the nerve elements, the more is this stability likely to be affected by toxic influences and by undue peripheral excitation.

It is important to bear in mind that the nerve elements do not readily rest when they are exhausted and badly nourished, and the value of providing an adequate and assimilable diet, and of the use of the stimulants alcohol and strychnine in the treatment of the insomnia which is associated with conditions of malnutrition, cannot be over-estimated.

The detection of errors in the way of living and of defects in hygiene and the rectification of these is the first duty of the physician. Over-work, late hours, depressing psychic influences of many kinds, lack of fresh air and exercise, irregularities of diet, the abuse of alcohol, tobacco, tea and coffee, and the abuse of drugs, especially of morphine, cocaine and veronal, are among the more common factors of insomnia. A simple regular life is essential, in which excitements and worries are as far as possible avoided, with a carefully planned diet, and the entire abrogation of alcohol, tea and coffee, tobacco and drugs, and with abundant fresh air and such regular exercise as the patient can take without undue fatigue.

The removal of the patient to fresh surroundings and a different atmosphere often has a most salutary effect in breaking the habit of sleeplessness. In some instances high altitudes, in others low-lying districts or the seaside, have the best effect. It must be borne in mind that the effect of change of atmosphere is not always immediate and the patient must therefore be warned against initial disappointment.

Mental activity should not be excited towards the hour of rest, and no active mental or physical work should be allowed after the evening meal, which should be taken early. The patient should go to bed early and rise betimes, and he should be encouraged to fight against the habit, which is common in insomniacs, of sitting up late, lying awake for hours and then sleeping late into the morning.

It is often an advantage in severe cases to treat the patient for a time in a Nursing Institution where he can be watched and have the benefit of regular hours and discipline, and where the precise degree of the insomnia can be discovered. This is an important point to determine, for it will be often found that patients sleep much more than their statements would bear out, though the sleep may be light and restless.

The advantages of a modified rest cure in many cases, and especially in those where there is malnutrition, and when neurasthenia is present, as well as in those in whom the insomnia is the result of shock, grief and worry, cannot be overestimated. Massage, electrical treatment and baths are generally of advantage, but the patient should never be isolated nor deprived of literature and such amusements as serve to pass time. Such a cure should last at least four weeks, and towards the end of this period if the patient is progressing satisfactorily, outdoor exercise and amusements generally aid his progress. It should be

followed always by a complete change and holiday lasting a month.

Symptomatic Insomnia.—The employment of drugs in this condition should always be subsequent to the application of those measures which tend to rest and comfort the region from which the pain or the discomfort are proceeding. A comfortable bed and pillows so arranged that there can be no pressure upon painful regions, the swathing of such regions in thick layers of cotton wool, the use of leeches and of icebags and of hot applications in the form of stupes, fomentations, poultices or electric pads, soothing liniments and the lowering of conditions of pyrexia by sponging, etc., should be employed wherever possible before any drug is given. When insomnia is caused by pain associated with marked anxiety or with shock, as, for example, in pericarditis and after severe injuries, morphia is always indicated. Morphia again is the only reliable drug when pain is above a certain degree of severity. Aspirin is one of the most valuable drugs in the treatment of insomnia due to pain and bodily discomforts generally. It may be given in doses of from 10 to 20 gr. and may with advantage be combined with 2 or 3 gr. of veronal. Alcohol is an excellent soporific in the insomnia of febrile states, of anæmia and of conditions of exhaustion, and should be given as a single full dose at night. In conditions of exhaustion it must be remembered that a patient may be too weak to sleep and that then hypnotics are contra-indicated, but the desired result may be brought about by the administration of stimulants in the form of readily absorbable food, alcohol and strychnine. For example—in cases of severe chorea where swallowing has become impossible, complete insomnia from the starvation and exhaustion is the rule, and this insomnia is unaffected by hypnotic drugs, but it readily responds to a good meal containing alcohol, administered by the nasal tube. Veronal is one of the best hypnotics in all conditions, but it is often given in too large doses. It will be invariably found that a small dose of veronal combined with either aspirin, phenacetin, phenazone, antifebrin or any other of the coal-tar analgesics will act much more efficiently than will a larger dose of veronal given alone. It should never be given in larger doses than five grains, and often a dose of three grains combined with an ordinary dose of one of the above-mentioned drugs will be found sufficient. It must not be forgotten that even small doses of veronal have proved fatal, that the drug is apt to produce temporary glycosuria and peculiar mental states and that a "veronal habit" is easily set up. It is essential that free action of the bowels is insured when this drug is administered. Medinal is a soluble derivative of veronal and is similar in its qualities. Hedonal and adaline are similar in their action to veronal. They are less potent and less toxic and may be given in ten-grain doses. Chloralamide is a gentle hypnotic and analgesic and is useful in mild cases. It is given in doses up to twenty-five grains.

Chloral is perhaps the best hypnotic of all where insomnia results from irritating conditions of the skin. Paraldehyde is one of the safest and most reliable hypnotics, but having no pain-relieving action, it is not of itself generally applicable to conditions of symptomatic insomnia, but when aspirin or some other analgesic drug is given in addition it is very useful. It is essentially a stimulant hypnotic and is admissible in every condition of disease, but from its action in increasing the bronchial secretions its prolonged use in old people should be avoided. On account of its disagreeable smell and taste it is usually prescribed in gelatine capsules containing twenty and thirty minims. The ordinary dose for an adult is one drachm. Some patients can take it readily when well diluted with peppermint water. Extract of liquorice conceals the taste to some extent. Amylene hydrate (dose 5–10 min.) and dormiol are similar in their action to paraldehyde.

Hyoscine is the most powerful of all the hypnotics we possess and it is a powerful analgesic. In appropriate doses it does not appear to be a dangerous drug and it acts well in combination with morphia. It is especially useful where morphia fails or is ill borne or is contra-indicated and when delirium is present. The dose is from $\frac{1}{200}$ to $\frac{1}{50}$ gr. Hyoscine does not keep well in solution and should therefore be used in tabloid form. The potency of a dose given is readily ascertained by the immediate dilatation of the pupils that follows administration.

The bromides are nervine sedatives, but they are not hypnotic nor analgesic drugs and are therefore of little value in symptomatic insomnia. Sulphonal, tetronal and trional are useful hypnotics which have little or no analgesic qualities. The former has fallen out of use on account of its slow action and its causal relation to fatal hæmatoporphyrinuria. Chloretone is a depressing remedy which has little to recommend it. A severe form of peripheral neuritis is a definitely known result of its administration.

Intrinsic Insomnia.—The treatment of this condition where no toxic state is discoverable and when senility is not the essential factor must be preceded by the most thorough investigation of the patient's bodily health, of his manner of life and of his mental state. All abnormal conditions of bodily health and

nutrition must be radically treated. The manner of life should be fundamentally changed, for the time at least both as regards work, relaxation and surroundings, and the examination of the mental state may reveal conditions of neurasthenia, psychasthenia or hysteria which should be treated, or some grief at heart which can be mitigated by discussion and advice. Above all the patient must be reassured and comforted, for in this malady particularly, "He is the best physician who gives most hope."

The condition of the insomniac upon retiring to rest is usually that he has a rapidly changing and unbreakable train of unpleasant thought, and an undue consciousness of the action of his heart, often with palpitation and cold extremities. He should be trained to avoid intellectual activity towards the hour of rest and to adopt some peace-producing form of amusement such as light reading, pleasant conversation, sedentary games, listening to music, etc., before he retires. Massage and either hot or cold baths are often productive of an immediate peacefulness that will induce sleep. Various tricks for breaking the train of thought and concentrating the attention towards monoideism, such as taking slow deep breaths until a large number of respirations have been counted, striving to keep the eyes open as long as possible, repeating monotonous rhymes, etc., are sometimes of great value. The patient should sleep upon a hard bed lightly covered and kept warm, and with plenty of fresh air. Sometimes sleeping in the open air is of signal benefit. Absolute quiet must be assured during the early hours of rest.

Gastro-intestinal irritation is so frequently a factor in the production of insomnia that especial attention must be directed towards the alimentary canal. The relation of meals to the hour of rest should be altered and the composition of the meals changed. Flatulency and fermentation should be treated with intestinal antiseptics, such as acetozone, $\frac{1}{2}$–ii gr., and calomel, $\frac{1}{6}$ gr., or naphthalene tetrachloride 10 gr. in cachets. Constipation especially must be avoided, and the preparations of aloes will be found as valuable in the treatment of insomnia as they are in the treatment of night terrors.

Certain general remedies which act as calmatives are of great value. Foremost among these stands sodium bromide in ten-grain doses thrice daily combined with strychnine and glycerophosphates. This drug does not act as a hypnotic, but it increases the stability and lessens the irritability of the nervous system. Another most useful general remedy is aspirin given regularly in ten-grain doses three times a day after meals.

Many minor measures such as the use of a hop pillow or a scented pillow, the eating of lettuce or of onion at the evening meal, a half glass of strong ale or stout and a glass of hot milk before going to bed are sometimes surprisingly efficacious.

In the treatment of nearly all cases of insomnia some drug must be given in the first place to relieve the patient's immediate distress. It will be necessary to probe his knowledge and note carefully his experience of hypnotic drugs, which is apt to be wide, and subsequently to ignore his statements that any drug is not efficacious, and in no circumstance to allow the patient knowledge of what drug is being given. Morphia should be as far as possible avoided and reliance placed upon aspirin, the various coal-tar derivatives and veronal, the great value of combinations of these drugs being carefully borne in mind. Any of the drugs that have been mentioned for the treatment of symptomatic insomnia may be used, but it is important to ring the changes among the hypnotic drugs and not to persist with any one drug. When a hypnotic is given it should be in such a dose as will certainly produce sleep, and after a good night's rest has been secured the hypnotic should be replaced by a placebo on the following night. It must not be forgotten that idiosyncrasy with regard to hypnotic drugs is common and that a mild remedy will not uncommonly succeed where a stronger remedy has failed.

Toxic Insomnia.—When resulting from a drug habit this condition can only be dealt with successfully by using the strongest measures for the rapid eradication of the habit. Where alcoholism is the causal factor, complete abstinence with careful attention to the nutrition and the use of paraldehyde as a hypnotic are essential and a course of strychnine and bromides very helpful. In the sleeplessness of delirium tremens, paraldehyde in full doses and hyoscine where the former fails are the best remedies, a liberal and assimilable diet being the essential factor for recovery. In febrile toxic conditions insomnia calls for the administration of alcohol and other stimulants, and especially is this the case when low delirium is present, as, for example, in enteric fever. In some cases of uræmia sleeplessness is a most distressing symptom, and this is best relieved by the use of morphia in doses of $\frac{1}{6}$–$\frac{1}{4}$ gr. When high arterial tension is present the usual methods of treatment should be employed, but when in addition there is marked arterial sclerosis a stimulant line of treatment should be adopted and no attempt should be made to lower the arterial tension, since in these circumstances the insomnia is probably the result of an insufficient cerebral blood supply due to

the arterial sclerosis and a relatively failing heart. In either case any of the milder hypnotic drugs are admissible.

Senile Insomnia is closely allied to that of arterial sclerosis. Cardiac stimulants in the form of a carefully planned diet, alcohol and strychnine are indicated. A full dose of alcohol at the hour of rest is often the best hypnotic.

J. C.

INFANTILE CONVULSIONS AND NIGHT TERRORS

Infantile Convulsions.—Convulsions in the infant may be the result of some general toxæmia, or of gross organic disease of the nervous system. In the former condition the convulsions are readily amenable to treatment: in the latter they may be controlled for a while, but are liable to recur.

The rectum should be washed out with saline solution, and if the convulsions are not immediately arrested, three to five grains of chloral and ten to fifteen grains of bromide should be given in one ounce of water as an enema to an infant under six months of age. A warm bath may be given, and cold applied to the head. If after half an hour the convulsions still continue, chloroform should be administered in sufficient quantity to keep the convulsions in control. After four hours the bromide and chloral may be repeated. Nothing should be given by the mouth while the child is in convulsions. A lumbar puncture should be performed, not only for diagnostic purposes, but also for the relief of intra-cranial pressure. Cessation of fits not infrequently follows this procedure especially in such conditions as whooping-cough and those in which there is marked cyanosis and cerebral congestion. The application of *leeches* is of service in those cases in which there is marked cyanosis. The leeches are usually applied behind the ear. Such drugs as nitrite of amyl, hyoscine and morphia are advocated by some authorities, but though they may be effectual in staying the fits, the depression which they produce is often difficult to combat.

The after treatment of an infant who has had a series of convulsions is most important, and the general hygiene and diet must be attended to. The continued administration of small doses of bromide is also advisable, the amount of bromide being steadily diminished and eventually omitted altogether. Infantile convulsions are in some cases the earlier manifestation of epilepsy, the treatment of which is dealt with elsewhere.

Night Terrors.—In dealing with a child subject to night terrors it is of first importance to remove any cause which may give rise to disturbed sleep. The size, ventilation of the bed-room, the bed, the covering and the night apparel all need attention. The diet also must be carefully regulated. The child should not be allowed to suffer hunger, nor must it be fed shortly before going to sleep. Tonsils, adenoids, worms, constipation, over-work at school, may all be the cause of night terrors, and must be attended to. When all these possible causes have been treated and the night terrors still persist, sedative drugs may be administered. One of the salts of bromide is probably the best sedative for such cases, alone or combined with some carminative, bismuth, gentian or rhubarb. Sodium or potassium citrate with some spiritus ætheris nitrosi is also a useful remedy. Small doses of hyd. c̄. creta should also be given. Other sedative drugs which are of value are 5 to 10 gr. of urethane and 2 to 5 gr. of aceto-salicylic acid.

Change of air and surroundings are essential in those cases in which the symptom is the result of undue anxiety about work at school.

F. E. B.

TICS

A tic is more than a mere stereotyped act or mannerism. A stereotyped act or stereotypy is a normal movement repeated involuntarily at certain times, as when an individual puts out the tip of his tongue when he writes. A tic is an exaggeration of a normal movement. It is "a co-ordinated purposive act, provoked in the first instance by some external cause or by an idea; repetition leads to its becoming habitual, and finally to its involuntary reproduction without cause and for no purpose, at the same time as its form, intensity and frequency are exaggerated; it is often convulsive, inopportune and excessive. Its execution is often preceded by an irresistible impulse, its suppression associated with malaise. It occurs in predisposed individuals, who usually show other indications of mental instability."

General Treatment.—It is desirable to pay due attention to eyes, ears, nose, teeth, etc., as some trifling source of peripheral irritation may be acting as a stimulus perpetuating the tic. Clothing must not be ignored. Some head-nodding tics in girls are undoubtedly associated, at least in the beginning, with large and unwieldy hats. Imitation is a fertile cause of tics, hence the question of the patient's environment should be considered.

Medicinal Treatment.—Sedatives and hypnotics sometimes effect a transient improvement, but they cannot permanently modify the psychical defect at the basis of the disease. Sometimes good results are obtained, especially in children, with the bromides. Zinc valerianate and other preparations of valerian have sometimes proved advantageous. Quinine, cannabis

indica and arsenic have also been tried. Massage, mechanotherapy, hydrotherapy, electrotherapy, hypnotic suggestion, have all had their votaries in the treatment of this affection. The last-named has sometimes given tangible results. Favourable results have followed the adoption of suggestion during waking hours, but the method is certainly not of universal applicability. It may well be asked, moreover—as do Meige and Feindel—what exactly is meant by suggestion : " To encourage the patient and assure him of progress, to reproach or reprimand him on occasion, is to employ an integral and valuable factor in all re-educational treatment of tics, but is this truly suggestion ? "

Treatment by Re-education.—Systematised mental discipline, *i. e.* education of movements by some form of drill, is the method *par excellence* for the treatment of tic. Brissaud's method is a combination of immobilisation of movements with movements of immobilisation. Some exercises are intended to teach the patient to preserve immobility, others to replace an incorrect movement by a normal one. It is essential to remember that they must be graduated. In the first group of exercises, the patient is required to preserve complete immobility for a second or two, or more—in fact, as long as he can without fatigue. Very gradually the period is increased. The treatment should take place regularly several times a day, at regular hours. The physician should always encourage the patient by affirming that he can and must remain immobile. It is a good plan to take the exercises in front of a mirror, whereby the patient can appreciate the degree of immobility attained. In the second group, the patient is required to make slow, regular and accurate movements to order, attention being devoted to the muscles involved in the tic. The performances should be gone through several times daily, always at the same hours; fatigue should be avoided; and to begin with, the exercises should be short and simple. The use of a mirror for this drill is very desirable. Even though the tic disappear, the patient should be encouraged to continue his exercises. The following is a specimen of treatment for a facial tic, given by Meige and Feindel : " Every day, and three times a day, at the same hours—nine, one and six—the patient is to look at himself in a mirror, preserving absolute immobility the while; to read aloud for two minutes, to speak in front of the glass for two minutes, to walk backwards and forwards in front of the mirror for two minutes. During the ten minutes of these exercises he will endeavour to keep his facial musculature under control. If the tic asserts itself in the course of one of the exercises, he will begin again, if necessary twice; the third time he will leave it till the next séance." Here is another specimen of treatment for a case of mental torticollis : " Stand or sit in front of a mirror and endeavour to maintain an absolutely correct position of trunk and shoulders. Lift the arms vertically and turn the head to the right, then lower the arms while the head remains as it is. Bend the body forward, and stretch the arms out till they touch the ground, the head meantime being rotated to the right. Then rise up again with the head in the same attitude. After two or three efforts it will be found that the head can be kept straight for a few seconds." Systematised exercises of any sort are of value in the treatment of tics. It is the bestowal of the attention on the allotted task that has such a salutary effect. All re-education procedures are modelled on the same plan; the practitioner will readily be able to prescribe treatment along these lines to suit particular cases. Where the arm is involved in a tic, simultaneous employment of both arms and hands in various exercises—writing, drawing, painting, tracing, etc.—is often extremely useful. The simultaneous execution of movements by both limbs results in the sound limb imposing regularity on the other. It is always desirable to vary the procedures and to render them as interesting as possible.

Occupation Neuroses and Craft Palsies

The class of occupation neuroses is a very comprehensive one, including as it does all cases in which certain symptoms follow the attempt to perform some act which has become more or less automatic. These symptoms are usually of the nature of pains, painful cramps, spasms or contractions; they occur in the case of writers, typists, violinists, telegraphists, seamstresses, flutists, cigarette-makers, turners, tailors, letter-sorters, and in many other occupations where the muscles of the hands and arms are involved; similar neuroses occur in glass-blowers, in players of clarionets and other wind instruments, involving other sets of muscles. In all these neuroses the mental element is pronounced. The more the attention is directed to it, the greater the intensity of the cramp. As a rule, the groups of muscles involved can be innervated with ease for any other movement than the professional one.

It must be candidly admitted that many cases of occupation neuroses are very obstinate. Drugs are of but minor value. In the treatment of writer's cramp the patient must give up the use of his right hand for writing for a space of not less than three months. During that time he should learn to write with his left hand. After the prescribed interval—which, if practicable, may well be increased to six

months—the patient may begin to write again, and may use a Nussbaum's bracelet, or a thick cork penholder, holding it not too near the end, or he may put the holder between the index and second finger instead of between the index and thumb. Often good results are obtained by his using both hands simultaneously for writing, forming the letters in the copybook style, large and round. It is absolutely essential to avoid fatigue in the small muscles of the hand, and advisable, therefore, to make the movements slow and from the elbow or shoulder. In addition, a system of carefully graduated active and passive and resistive movements for the affected groups may be recommended. Massage is of comparatively little value. Sedative galvanism, or galvano-faradism, is often utilised, with but dubious results, however, in my experience. Undoubtedly the best line of attack in these difficult cases is one which is calculated to re-educate the will and increase the patient's power of inhibition. In the craft palsies, there may be an actual organic lesion produced—neuritis and muscular atrophy from pressure on nerves and muscles—and these cases are sometimes distinguished as occupation neuritis. It is important to recognise the cause at as early a stage as possible, and to enjoin complete cessation from the harmful trade for a time. When the lesion is definitely organic, treatment with massage and faradism is the best line to pursue.

The general principles already laid down for the treatment of writer's cramp are applicable to other forms of occupation neurosis.

S. A. K. W.

FAMILY PERIODIC PARALYSIS

1. One form of periodic paralysis has been met with in malaria, though not familial. In this variety quinine has proved effective.

2. The familial type of the disease is met with in childhood, but has a maximal incidence between the ages of twenty and forty, and tends to recur less frequently as age advances. It is not very amenable to treatment.

The onset of an attack seems to be determined on occasion by eating largely of rich and indigestible foods, or excessive muscular exertion. Hence the diet should be plain and wholesome, and exercise be undertaken in moderation.

Bromide, combined with caffeine and potassium citrate has been found useful. Tincture or infusion of digitalis has also been recommended. Electrical treatment in the form of faradism is also stated to prove beneficial, but as the affected muscles lose their excitability to both faradic and galvanic currents, its application has evidently a limited field of usefulness.

Constipation must be most carefully avoided in a predisposed individual, and the action of the skin and kidneys encouraged by free administration of fluids, such as Imperial drink, or whey.

C. M. H. H.

MYASTHENIA GRAVIS

Hitherto the cause of this mysterious disease has remained obscure, and its treatment is necessarily symptomatic. In acute cases all muscular exertion must be limited as much as possible, and nutrition must be maintained by liquid, concentrated foods—best given in the earlier parts of the day when the patient is least fatigued. Respiratory failure must be treated by artificial respiration. In the more chronic cases it is important to maintain nutrition by good food, malt, cod-liver oil, etc.: Organotherapy has at times seemed to do good, but its value is uncertain—strychnine, and arsenic and iron are useful: massage and electrical treatment is contra indicated.

C. M. H. H.

ACUTE INFECTIVE DISEASES OF THE NERVOUS SYSTEM

Meningitis

The treatment of meningitis depends upon the nature of the infection giving rise to the disease. The cause of the meningitis can usually be ascertained by means of lumbar puncture, and the examination of the fluid obtained from it, the nature of the cell contents and organisms. If no causal organisms are found the meningitis falls into the group of serous meningitis, or meningism.

Meningitis may be Meningococcal, Pneumococcal, Tuberculous, Streptococcal, Staphylococcal, Influenzal, Gonococcal, Streptothricial, Syphilitic Serous Meningitis, Traumatic or due to the Typhoid group of organisms.

General Treatment.—The acute symptoms occurring in meningitis, headache, fever, vomiting, restlessness, delirium and convulsions are relieved by rest, exclusion of sound and light, careful dieting, cold-application to the head and round the neck, the application of leeches behind the ear and such drugs as bromide and chloral given by the mouth or rectum. In some cases in which the convulsions will not yield to bromide and chloral, inhalations of chloroform should be used.

Meningococcal Meningitis.—There are probably at least two strains of the organism which give rise to meningococcal meningitis. These vary in their virulence, but any case in which the meningococcus is found to be present should be treated by the injection of a serum. The following anti-meningococcal sera can be obtained, that of the Lister Institute, of Flexner, of Kolle and Wassermann and Ruppel.

The method of injection is as follows: a lumbar puncture is performed and the cerebro-spinal fluid allowed to escape until all excess of pressure is relieved. The amount which escapes may be 30 to 60 c.c., and an endeavour should always be made to obtain at least 10 c.c., the amount of serum to be injected. The serum and the syringe with which it is injected should be warmed to the body temperature and the serum slowly injected into the vertebral canal. The bed should now be tilted so that the caudal end of the vertebral canal is at a higher level than the cervical region, in order that the serum, which is of a greater specific gravity than the cerebro-spinal fluid, may gravitate towards the brain. These injections should be repeated every day, and the cerebro-spinal fluid withdrawn on each occasion should be carefully examined, both cytologically and bacteriologically. As improvement takes place the fluid becomes clearer, the polymorphonuclear cells fewer, the lymphocytes relatively increased and the meningococci fewer and more difficult to cultivate. Three injections are usually required, but the number must depend on the effect of the serum on the organism.

The treatment of the later stages of the disease when all the acute symptoms have passed is one of some importance. A few cases recover rapidly and completely, others only slowly regain their normal health after two or more years. Some cases develop hydrocephalus, owing to the closure of the connection between the lateral ventricles and the spinal canal by adhesion in the iter between the third and fourth ventricles or around the fourth ventricle. Various methods have been devised for dealing with this form of hydrocephalus. The operation of making a connection between the posterior horns of the lateral ventricle and the subarachnoid space by means of strands of silk ligatures is probably the most satisfactory.

Pneumococcal Meningitis. — This form of meningitis is commonly the terminal result of a general pneumococcal infection, and is invariably fatal. A pneumococcal meningitis which is primary in the membranes should be treated by lumbar puncture to relieve the pressure, and by the injection of an anti-pneumococcal serum (Pane). Success has been reported in a case treated by this method (*Lancet*, 1912, II, 1294). Vaccines have been tried, but neither on theoretical nor practical grounds is any success from their use to be expected.

Tuberculous Meningitis.—No case of meningitis should be finally designated as tuberculous unless tubercle bacilli have been demonstrated in the cerebro-spinal fluid. An excess of lymphocytic cells is in a child in favour of the diagnosis tuberculous meningitis, especially when combined with other chemical and cytological changes in the cerebro-spinal fluid; but an increased number of lymphocytic cells may be found in early cases of poliomyelitis, in thrombosis of veins or sinuses, in late cases of meningitis of infective origin and in syphilis.

When once the diagnosis of tuberculous meningitis is confirmed, the treatment can only be directed to the relief of symptoms. Lumbar puncture will often relieve the headache, and temporary improvement occurs after its performance. Convulsions are stayed by chloral and bromide given either by the mouth or rectum. Vomiting is controlled by careful feeding, and if excessive, by washing out the stomach. It may be necessary in some cases to feed the child with a tube.

A few cases of undoubted tuberculous meningitis are on record in which recovery has taken place. The lines of treatment in these cases have been most varied, viz.: drachm doses of potassium iodide every four hours, leeches over the mastoid process, repeated lumbar puncture and the injection of a solution of iodine in iodide of potassium into the vertebral canal.

All these methods have failed in my hands, as well as others, such as inunction of mercury, the injection of silver salts, the administration of tuberculin and removal of a large portion of the skull for the relief of pressure.

Influenzal Meningitis. — The fluid obtained by lumbar puncture from a case of influenzal meningitis is commonly turbid, contains numerous polymorpho-nuclear cells, and unless cultivated on a medium containing blood serum is liable to be reported as sterile, although intra- and extra-cellular organisms may be seen in stained films of the fluid. The influenzal meningitis can only be distinguished from other forms of infective meningitis by a careful bacteriological examination.

This condition should be treated by large doses of hexamethylenamine (urotropine). Ten grains of this drug may be given every four hours to quite young children, and in a few cases recovery has followed. This line of treatment should be combined with lumbar puncture and other methods already suggested in cases of meningitis.

An anti-influenzal serum has been prepared by Flexner; but the results of treatment with this serum have not yet been worked out.

Meningitis due to other organisms, such as streptococcus, staphylococcus, the typhoid group, gonococcus, must be treated on the ordinary lines. In typhoid meningitis the proportion of recoveries is considerable, whereas in the other forms the mortality is very high.

Syphilitic Meningitis. — This form of meningitis occurs both in the adult and the child; but presents as a rule somewhat different symptoms. In the child there is commonly a

slowly progressive degeneration; whereas in the adult the symptoms are commonly more localised and give rise to localised weakness, and it may be atrophy of one or more limbs.

The diagnosis depends upon a high lymphocytic cell content in the cerebro-spinal fluid, and a positive Wassermann reaction both in the blood and cerebro-spinal fluid or in the blood alone. The cerebro-spinal fluid contains an increased amount of albumen.

The adult cases often respond strikingly to the administration of salvarsan, the inunction of mercury and the administration of potassium iodide.

The cases in infancy and childhood do not respond well to the above remedies, and the results obtained from this line of treatment are not encouraging.

Serous Meningitis.—This name is applied to a condition in which symptoms of meningitis are present and in which the cerebro-spinal fluid shows an increased number of lymphocytic cells, but no organism either on direct or cultural examination.

The condition commonly occurs in connection with some infective process in the body, the ear often being the source of that infection: a sinus or venous thrombosis will give rise to alteration in the cerebro-spinal fluid, which resembles that of serous meningitis. Serous meningitis also occurs in association with nephritis.

The treatment must depend on the cause. The removal of the source of infection is of the first importance. The symptoms can at times be relieved by lumbar puncture, and these cases can often be successfully treated by repeated lumbar puncture even when the direct cause of the disease cannot be ascertained.

Meningism. — This name is applied to a condition in which symptoms of meningitis are present, but in which the cerebro-spinal fluid chemically, cytologically and bacteriologically appears perfectly normal. Such symptoms often occur in association with the onset of the acute specific fever and pneumonia. Apart from lumbar puncture and the treatment of the various meningeal symptoms as they arise, meningism calls for no active treatment. These cases usually recover.

Acute Infective Myelitis

This commonly arises in connection with infection of the urinary and genital organs, such as a gonorrhœa or infection of the bladder. It is seldom possible to diagnose an infection of the spinal medulla apart from one in which the membranes are likewise affected, and most cases of acute infective myelitis are cases of meningo-myelitis. On the other hand, cases of infection of the membranes, the spinal medulla being but little or not at all affected, are by no means uncommon.

A paralysis of an ascending character is a striking symptom of some cases of acute infective myelitis.

The treatment of the acute stages consists in complete rest, preferably on a water bed, the administration of urotropine, attention to the bladder, rectum and back, and the removal and treatment if possible of the cause of infection.

In the later stages of the disease massage, active and passive movements and electricity is the treatment required.

Landry's Paralysis

It may be questioned whether a true Landry's paralysis ever recovers. Other forms of acute ascending paralysis, such as that which occurs in acute polio-myelitis and in meningo-myelitis, do undoubtedly cease to extend, and recovery, more or less complete, takes place.

Cases of recovery in Landry's paralysis have been recorded, but the evidence that they were cases of this nature is incomplete.

Apart from complete rest in bed, general nursing attention, and the treatment of pulmonary and cardiac complications as they arise, it cannot be said that any treatment for Landry's paralysis exists. F. E. B.

Note.—For Polio-myelitis, see "Specific Infectious Diseases."

SYPHILITIC DISEASES OF THE NERVOUS SYSTEM

Introduction. — Since the introduction of clinical pathological methods in the investigation of syphilitic disease of the nervous system, much has been learned as to the nature of the process and the problem has been attacked from all sides with fresh vigour. Further, the introduction of salvarsan in the treatment of syphilis has stimulated inquiry as to its effect in syphilitic nervous disease.

On the clinical side cases are diagnosed earlier than formerly, and their syphilitic nature recognised at a period before much structural damage has taken place. Patients, therefore, come under treatment with more prospect of cure and the physician has at his disposal means, not only of diagnosing the specific nature of the disease, but also of estimating the effect of treatment on the syphilitic process.

The trend of present studies is to lessen the distinction between cerebro-spinal syphilis and the meta- or para-syphilitic diseases, such as general paralysis of the insane and tabes, in that they are both due to the presence of the syphilitic organism in the nervous system. Their treatment, therefore, should have this in common—the extinction of the syphilitic organism whether in the body generally or

in the nervous structures. Formerly many authorities who advocated anti-syphilitic treatment in cases of cerebro-spinal syphilis, deprecated or damned with faint praise its use in cases of tabes or general paralysis. Their opinions were based upon the different histological appearances in the two conditions, and upon the apparent failure of mercury and iodide to relieve or check the progress of the latter. With modern methods, however, changes in the reactions to the Wassermann test and in the contents and character of the cerebro-spinal fluid have been proved to occur, not only in cases of cerebro-spinal syphilis but also in cases of tabes and general paralysis, and in some instances these have been associated with definite improvement in the clinical condition of the patients.

The reason why anti-syphilitic treatment is successful in cases of general syphilis, and may be more or less ineffectual in cases of syphilitic nervous disease, is not at all obvious. It may be that the drugs come in contact with the organism more easily when it is located in the body, and that they fail to reach it in sufficient quantities when situated in the nervous system. Or, on the other hand, the tissues of the body generally may be more resistant than those of the nervous system, or possess greater powers of producing anti-bodies. Chemical examination of the cerebro-spinal fluid has failed to demonstrate the presence of mercury, iodide or arsenic in the cerebro-spinal fluid. Goldmann has shown that the choroid plexus intercepts dyes which have been injected intravenously in large quantities, and that intravenous injections fail to stain the nervous system. On the other hand, by the injection of the stain into the cerebro-spinal fluid by lumbar puncture he was able to stain the whole cerebro-spinal axis with the exception of the cortex, the dye penetrating and staining all the neurones (Mott, *Brit. Med. Journ.* I., Nov. 15, 1913).

From the above it would appear possible that drugs which might be absorbed into the blood would exercise an effect on the body and yet have no effect on an organism situated in the nervous system. It might also be supposed that if the blood serum be capable of producing anti-bodies these would be more or less shut off from acting upon organisms situated in the nervous system.

Further, the anti-syphilitic effect may be produced chiefly by the reaction of the drug upon the serum. The effect of injecting the serum of syphilitic patients whose reaction in the blood has been rendered negative, into the cerebro-spinal fluid, is still in the experimental stage, but the results published are encouraging.

It is impossible, therefore, at present, to make any dogmatic assertions as to the efficacy of any special drug or mode of treatment, but the outlook is much more favourable and points to the necessity of anti-syphilitic treatment in all cases of syphilitic nervous disease irrespective of its type.

Diagnosis of Syphilitic Nervous Disease.—In view of the multiplicity of symptoms, which may arise in syphilitic disease of the nervous system, the possibility of any organic case of nervous disease being due to syphilis must ever be present in the mind of the physician. Formerly the evidence of syphilis was obtained from the history of the patient, the presence of syphilitic scars or by inference from the clinical symptoms, but since the introduction of the Wassermann reaction and the cytological and chemical examination of the cerebro-spinal fluid, further and more reliable means of determining the syphilitic character of a case have been provided.

The tests to be employed are four in number—

1. Wassermann reaction in the blood.
2. Wassermann reaction in the cerebro-spinal fluid.
3. Cytological examination of the cerebro-spinal fluid.
4. Chemical examination of the cerebro-spinal fluid.

1. **Blood. Biological Tests of the Blood. Wassermann Reaction.**—This test, although specific for syphilis, may yield a positive reaction in a small number of cases of malaria, sleeping sickness and scarlet fever. A positive reaction is present in the blood in most cases of early syphilis of the nervous system; in a relatively large number of tertiary and parasyphilitic cases, however, it may not be obtained. This may be due to the effect of previous treatment or to the reaction of the untreated patient to the syphilitic virus.

The Wassermann reaction in the blood, therefore, cannot be used as an isolated test for the diagnosis of syphilis of the nervous system as: (1) It may be present in cases of syphilis in which the nervous symptoms are due to some other cause; (2) it may yield a negative reaction in cases of syphilitic nervous disease. Whether the Wassermann reaction in the blood can be taken as a guide to therapy or as an indication of cure is yet undecided, but, on the whole, experience shows that a repeated negative reaction indicates that anti-syphilitic treatment has been successful as far as the syphilitic infection of the body is concerned.

2. **Wassermann Reaction in the Cerebro-Spinal Fluid.**—This test is of greater significance than the blood test in cases of syphilitic nervous disease. A positive reaction is found in 99 per cent. of cases of paresis, in all cases of active meningeal syphilis, and in 70–80 per cent. of cases of tabes. In other forms of nervous syphilitic disease the percentage is very variable.

3. Cytological Examination of the Cerebro-Spinal Fluid.—The examination of the cell content of the cerebro-spinal fluid is of great importance, not only from the point of view of diagnosis, but also of prognosis. Lymphocytes are found in most chronic inflammatory processes, and in cases of syphilitic nervous disease are present in increased numbers. The degree of lymphocytosis present depends upon the activity of the syphilitic process and the situation of the lesion; the more acute the condition the greater the number of cells, more especially when the meninges are involved. Lymphocytosis may be present before the onset of any very definite clinical symptoms. A reduction in the number of lymphocytes may be taken as an indication that treatment is having a beneficial effect; it may be noted after mercurial or arsenical treatment. Lymphocytosis may be present in any chronic inflammatory condition, and is, therefore, not confined to syphilis, but its importance as a corroborative sign cannot be over-estimated.

4. Chemical Examination. — An increase in the globulin in the cerebro-spinal fluid bears a close relationship to the degree of lymphocytosis, but may be present in cases of spinal compression and in some acute diseases. The value of an increase of globulin as a diagnostic sign therefore depends on co-existing conditions.

Methods of Anti-Syphilitic Treatment applicable to the Treatment of Syphilitic Disease of the Nervous System

Mercury

Mercury may be administered by (1) inunction, (2) injection, or (3) by the mouth.

1. **Inunction.**—This method is the one employed at Aachen (Aix-la-Chapelle) and has proved most satisfactory. Its application is simple, and, if properly supervised, can be quite efficiently carried out at home or at different spas in this country. The disadvantages of employing this method at home are its inconvenience and the difficulty of preventing the patient's relations from becoming aware of the nature of his illness. Its advantages are the rapidity with which the patient can be brought under the influence of the drug and the fact that it rarely causes gastro-intestinal disturbance. The duration of the course of inunction, the dosage and the frequency of the rubbings must be determined in each case by the urgency of the symptoms and the tolerance of the patient to the drug. It is essential to attend to the hygiene of the mouth. The teeth should be brushed after meals, first with tooth-paste and then with a solution composed of one part of a 10 per cent. solution of peroxide of hydrogen freshly prepared in six parts of water. In order to harden the gums a 2 per cent. solution of aluminium aceto-tartrate should be used as a mouth-wash and gargle.

The patient should be weighed every week and his urine tested for albumin, as a rapid loss of weight or the appearance of albumin are indications that the treatment should be suspended.

Inunctions should be given if possible by a skilled rubber, but if the patient is to inunct himself he must be carefully instructed as to the method of inunction, and the treatment must be supervised. He should be given a warm bath before each inunction, the best time for which is at night before going to bed. The ointment should be rubbed in for from fifteen to twenty minutes, the application being made to different parts of the body in rotation; hairy parts should be avoided, and the following areas will be found to be the most suitable—the flexor surfaces of the arms and legs, the inner surfaces of the thighs, the groins and the back. The rubbing is best performed with the naked hand, otherwise a rubber glove or glass rubber may be used. After the inunction the part inuncted should be wrapped in a flannel bandage. The following ointments are the most suitable: unguentum cinereum, composed of equal parts of mercury and lanoline with a sufficiency of olive oil, 1 dr. to be used at each inunction; blue ointment $1 - 1\frac{1}{2}$ dr., or 1 dr. of unguentum hydrargyri oleatis 10 per cent.

The duration of the course will vary in individual cases and may consist of from sixty to a hundred rubbings. The course may be interrupted after from twenty to thirty rubbings for a period of ten days, when they may be begun again, but when possible it is better to continue treatment until physiological effects are produced. If the patient's circumstances permit he may be sent to Aachen or to other spas at home or abroad, where the treatment is efficiently carried out. The advantage of Aachen is that the patients have sulphur baths before the inunctions, that the rubbing is given by skilled attendants, that the patients are obliged to lead quiet and routine lives, and that they are saved from the inconvenience of inquisitive friends. Inunction is obviously not a suitable method for hospital out-patients.

2. **Injection.**— Treatment by injection of mercury has certain advantages, it may be more convenient for the patient than a course of inunction, and in the case of hospital out-patients one can be certain that they are receiving sufficient dosage. Mercury can be injected in a soluble or insoluble form. Soluble preparations have to be injected daily or on alternate days as the mercury is rapidly eliminated; another objection is that the injection

is liable to be followed by pain. The most suitable soluble preparations as recommended by Mr. Campbell Williams are the sozoiodolate which should be freshly made—

℞ Hydrarg. Sozoiodol. gr. ii ss
Sod. Iodidi. gr. v
Aq. Dest. ♏ c

Dose: 10–20 min., containing $\frac{1}{4}-\frac{1}{2}$ gr. of the salt.

℞ Hydrarg. Succinimid. gr. ii ss
Aq. Dest. ♏ c

Dose: 10–20 min., containing $\frac{1}{4}-\frac{1}{2}$ gr. of the salt.

The insoluble injections need not be given more than once a week. Grey oil is the most suitable insoluble preparation, and the following is the formula which has been very successfully employed by Colonel Lambkin—

Pure Metallic Mercury gm. 10
Creo. Camph. 20 c.c.
(Equal parts of absolute creosote and camphoric acid.)
Palmitin basis to 100 c.c.

Ten min. contain 1 gr. of metallic mercury. Weekly injections should be given in a series of from six to eight or more, as required. Calomel injections are the most powerful of all mercurial injections; it is liable to cause pain, and to obviate that it should be given according to the formula recommended by Colonel Lambkin—

Calomel 5 gm.
Creo. Camph. 20 c.c.
(Equal parts of creosote and camphoric acid.)

Ten min. equals $\frac{1}{2}$ gr. of calomel. Dose: 10–15 min. as an injection once a week for not more than four weeks in succession.

The use of calomel is not to be recommended except in urgent cases, and grey oil will be found to be the most satisfactory form of injection. It is even more important carefully to watch the effect of treatment on the patient when treating him by injection than by inunction. In general the injection should be intramuscular, the favourite situation being into the gluteal muscles, the greatest care being taken to ensure antiseptic precautions, the avoidance of injury to the sciatic nerve and vessels, or of direct injection into any blood-vessel.

3. **By the Mouth.**—Mercury may be administered by the mouth in the form of pills, powders or mixtures. This method may be employed, but is not so satisfactory as either inunction or injection. The following prescription may be used—

℞ Hydrargyri Perchloridi gr. i
Potassii Iodidi ʒ iv–℥ i
Glycerini ℥ i
Aquam Destillatam ad. ℥ viii

Sig. a tablespoonful thrice daily after meals.

Iodide

Iodide.—Pot. iodide 5–30 gr. may be given thrice daily either in combination with mercury or separately at the same time. The addition of 3 min. of Liquor Arsenicalis will diminish the tendency to the iodide rash. Many authorities prefer to give iodide apart from mercury altogether, and to follow up a course of mercury with one of iodide. Iodide is specially useful in treating late tertiary syphilis. It should not be forgotten that in a number of instances large doses of iodide are better borne than small ones and prove more efficacious.

Arsenic

Salvarsan "606."—It is yet too early to speak definitely of the permanent effect of 606 in cases of syphilis of the nervous system. So far experience shows that it has a more rapid action than mercury and that, if given with proper care and discrimination, it is not attended by ill effects. It should not be employed in cases complicated by serious renal or cardiac disease. It is best given by intravenous injection, and the dose must depend upon the circumstances of each case, but as a rule 0·3 gm. may be given as an initial dose and afterwards increased to 0·4 and 0·5 or 0·6, the injections being repeated at intervals of a week or ten days. The mistake was made at first of only giving one or two injections, but experience has shown that many injections are necessary if any permanent effect is to be obtained. An exacerbation of the symptoms may follow the first or second dose, but this must not be taken as a contra-indication for further treatment.

Neosalvarsan "914."—Neosalvarsan has certain advantages over salvarsan in that it is soluble in water, forms a neutral solution, and does not give rise to any serious untoward symptoms if by any mishap some should be injected into the tissues. It requires no special skill in the preparation, but great care should be taken to prevent oxidation. Opinions vary as to the efficacy of neosalvarsan compared with salvarsan, but as far as my experience goes it seems to act equally well.

Salvarsan or neosalvarsan is specially useful in early cases of cerebro-spinal syphilis or where a rapid action is desired, and may be given in fairly large doses, but the immediate clinical improvement which is noted in such cases must not lead one to discontinue further anti-syphilitic

[1] *A System of Syphilis,* Vol. IV. p. 468.

treatment. In cases with more chronic lesions smaller doses should be used, the injections being repeated more frequently. The exacerbation of symptoms which were observed to occur in some cases after one or two injections are only temporary and subside if the treatment is persevered with. Although salvarsan and neosalvarsan have a more rapid action than mercury, the best results are obtained by using either of them in combination with mercurial treatment, the latter being commenced after the second injection and continued until a full course of mercury has been given.

T. G. S.

CEREBRO-SPINAL SYPHILIS

Under this term are included all cases in vhich the symptoms and signs present result 'rom syphilitic lesions in the brain, spinal nedulla or their membranes. Syphilitic lesions nay originate in the membranes or blood-ressels, and may involve any part of the central iervous system, or the cerebral nerves or pinal roots as they pass through the membranes. 'he pathological process, therefore, may vary onsiderably in its nature, and as the lesions nay be single or multiple and of wide distribuion the clinical picture presented differs widely 1 different cases.

The following is a brief summary of the various yphilitic lesions which may be met with corelated with some of their clinical symptoms.

Meningeal Lesions

Cerebral.—Gummatous Meningitis. Gumata, causing—

1. Cerebral nerve palsies—especially ocular aralysis.
2. Headaches—especially at night.
3. Fits, generalised or local, often Jacksonian type and associated with or followed by aresis or paralysis.
4. Hemiplegia, hemianasthesia, hemianopia, various monoplegias, mental impairment.
5. A combination of symptoms—simulating tracranial tumour or general paralysis.

Leptomeningitis or *syphilitic changes in the endyma* cause general symptoms of increased traeranial pressure often without local signs.

Spinal.—Pachymeningitis causing local root mptoms, motor and sensory, severe in degree d subacute in onset, followed rapidly by gns of compression of the spinal medulla.

Leptomeningitis, causing diffuse and indefinite ot symptoms of slow onset, followed by or sociated with slight symptoms of compression the spinal medulla.

Vascular Lesions

Cerebral, resulting generally in thrombosis, ich may give rise to slight and indefinite nptoms or to severe and obvious paralysis, hemiplegia, hemianæsthesia, hemianopia, aphasia, monoplegia, cerebellar or thalamic symptoms—usually of sudden onset but often preceded by premonitory symptoms.

Spinal, resulting in thrombosis, which may cause symptoms of "myelitis" or local intramedullary lesions (Brown-Séquard's syndrome), generally of rapid onset but usually preceded by definite premonitory signs.

Treatment

Prophylaxis.—It must never be forgotten that any person who has been infected with syphilis is liable to develop cerebro-spinal syphilis. It is obvious, therefore, that all cases of syphilis should be efficiently treated in the first instance, and should be examined from time to time to see whether there is any evidence of recrudescence of the disease. This is easier of attainment now-a-days than formerly, as the public have become imbued with the idea that it is now possible to tell whether a person is suffering from syphilis or not, and should he be, to cure him rapidly by means of "606." This idea has led many who have previously been infected or who have run the risk of infection to submit themselves for examination and has impressed on others the advisability of seeking immediate advice subsequent to any possible infection.

We cannot say that at present we possess any means of telling whether a case of syphilis has been cured or not. By the Wassermann test we can recognise the existence of active syphilis, but it cannot be said to solve the question as to the cure of syphilis, although it is undoubtedly of the greatest value as a positive sign. Provided its limitations are recognised its value as a negative sign should not be underestimated.

Treatment of Special Forms

1. Cerebral Gummata and Gummatous Meningitis. As a rule gummata present the general features of intracranial tumour—headache, vomiting and optic neuritis, but the symptoms develop more rapidly in from three to six months. The headache is usually more constant than in cerebral tumours and is often referred only to one spot. Optic neuritis may be very intense, and vision, as a rule, fails early, and the patient may become blind within five months of the onset of the symptoms. The local symptoms depend on the situation of the tumour.

Medical.—Active anti-syphilitic treatment with "606" or neosalvarsan, inunctions of mercury and large doses of iodide should be commenced at once, but if the symptoms progress or vision begins to deteriorate a decompression operation should be performed without delay.

Surgical.—Decompression will preserve the patient's sight and may even be necessary to save his life. Removal of the intra-cerebral portion of the growth should not be attempted, but dural gummata can be removed.

Surgical treatment will not cure the patient, but it may save him from blindness and permanent paralysis, and render it possible to give prolonged and effective medical treatment. Further, it is a well-established clinical fact, that anti-syphilitic treatment is often much more effective after operation than before.

2. **Basal Gummatous Meningitis.**—In this condition the patient is subjected to (1) pain and stiffness about the neck; (2) paralysis of various cerebral nerves; (3) symptoms of a rise of intracranial pressure—headache, vomiting, optic neuritis with which may be associated paralysis unilateral and bilateral. As in cases of cerebral gummata loss of vision may ensue very rapidly, and therefore active anti-syphilitic treatment should be commenced at once, and if the general symptoms are not relieved decompression should be performed without delay.

3. **Spinal Meningitis. Syphilitic Pachymeningitis.** It is not uncommon to find that anti-syphilitic treatment exerts little effect on the condition. Irreparable damage to the nerve structures, spinal roots and spinal medulla may result merely from the pressure effect of the meningitis, and therefore when there is no response to antisyphilitic treatment operation should be undertaken for the relief of pressure, the nerve-roots can be freed from adhesions and to a certain extent the spinal medulla also, and in this way saved from destruction. Further, this procedure will often render more effective the subsequent anti-syphilitic treatment, which should be persevered with and repeated subsequently as a routine measure.

4. **Spinal Leptomeningitis.**—In all cases active anti-syphilitic treatment should be carried out. If this does not suffice to clear up the symptoms and a definite level of compression can be determined, laminectomy should be performed, as it has been proved by experience that in many cases the spinal compression is due to the damming up of cerebro-spinal fluid, or to the local formation of an arachnoid cyst, and that simple opening of the membranes may result in complete recovery.

5. **Vascular Syphilitic Lesions.**—In the acute stages treatment with mercury and iodide is indicated in preference to salvarsan or neo-salvarsan. Instances of hæmorrhage occurring at the site of the lesion have been reported in cases where Salvarsan has been given soon after the onset of a vascular lesion. It is possible, however, that the hæmorrhage occurred as the result of a rise in blood pressure and without any direct connection with the Salvarsan. In the later stages there is no objection to using salvarsan or neo-salvarsan, but as a precautionary measure the dose should be small.

T. G. S.

TABES DORSALIS

The treatment of tabes dorsalis may be considered from three standpoints: (1) prophylaxis; (2) treatment of the disease; (3) treatment of the symptoms.

1. **Prophylaxis.**—There can be little doubt that without syphilis there would be no tabes dorsalis, and although the number of cases of syphilis in which tabes subsequently develops is relatively extremely small, yet serum and cytological tests confirm the idea that the disease is due to some action of the syphilitic virus upon the nervous system. This action probably only occurs when the infection has invaded the nervous system. Whether some forms of syphilis are more prone to produce tabes than others, or whether the nervous system in some cases is inherently more liable to be affected in this manner, are still open questions. Various other circumstances such as fatigue, illness and sexual and alcoholic excesses may, by reducing the vitality of the body and nervous system exert a bad effect on the disease when present, or render the patient more liable to develop it. There does not, however, seem to be any definite evidence that injury can produce the disease.

To prevent tabes, therefore, it is necessary to avoid syphilitic infection, and if such has occurred, to treat the syphilis thoroughly and so endeavour to free the system permanently from it. By means of the Wassermann reaction repeated at intervals it is now possible to judge more accurately whether this desired state has been arrived at or not.

2. **Treatment of the Disease.**—We are now able to recognise the disease in its earliest stages, and this enables us to attack it before there are many signs of organic affection of the nervous system. The first step must be the employment of active anti-syphilitic treatment and attention to the general hygiene of the patient. Anti-syphilitic treatment was formerly looked upon as of doubtful value, but at that time early cases were not recognised and recent reports of the treatment of early cases are very much more hopeful. There is no doubt whatever that genuine cases of tabes are alleviated and benefited by active treatment.

The form of treatment to be employed must depend a good deal upon the individual and his circumstances, but as a routine method he should be treated with arsenic in the form of 606 or neosalvarsan and later with mercury and iodide.

3. Symptomatic Treatment

Cerebral Nerve Palsies.—Ocular palsies are not uncommon and should be treated on anti-syphilitic lines. In the great majority of cases this will result in recovery, especially when the onset of the paralysis has been sudden.

Optic Atrophy.—Few symptoms are more distressing than the loss of vision which occurs in about 5 to 10 per cent. of cases and which is due to the onset of optic atrophy. Generally no treatment can stay the progress of this condition. Mercury and iodide have not been found to be of any use, salvarsan has been praised by some and condemned by others, but personally my experience has been that it does not do harm and that in some cases vision has been preserved and even improved. Salvarsan or neosalvarsan should be given in repeated small doses.

Laryngeal Paralysis.—Paralysis of the abductor muscles may occur alone or in association with laryngeal crises. It does not interfere with speaking, but may cause some dyspnœa or stridor, especially if from any local inflammation the vocal folds should become swollen. In cases with acute dyspnœa tracheotomy may be necessary.

Motor System.—Atrophy localised to certain muscles may be present in a relatively small number of cases and should be treated locally with massage, galvanism and faradism. A condition of general wasting combined with loss of muscular tone is not at all uncommon and may be benefited by massage and resistance exercises.

Ataxia.—The ataxia of tabes may be due to several causes, but chiefly to the loss of the sense of position, joint sense and deep sensibility. It is best treated by means of the exercises devised by Frænkel with a view to the re-education of the co-ordinating paths.

Before commencing treatment the patient must be examined in order to find out : (1) the nature of the sensory defect ; (2) its intensity ; (3) its distribution. This enables one to tell to what sensory defect the ataxia is due ; whether the defect is relative or complete and whether it is confined to the area of one or two joints, or widely distributed. The ataxia may be confined to the trunk and lower extremities and these cases may be divided roughly into groups.

1. Those who are unable to walk or stand.
2. Those who are unable to walk, but who can stand.
3. Those who can only walk with assistance.
4. Those who can walk alone, but whose gait is unsteady and who are made more unsteady when deprived of the aid of vision. In other cases the upper extremities may also be ataxic or the ataxia may be limited to them.

In addition to determining the sensory defect present in each case it is necessary to estimate the effect of hypotonia and joint changes on the gait and movements should such be present.

In all cases where the ataxia has limited the use of the limbs the muscles should be strengthened by means of faradism, massage and resistance exercises.

Fraenkel's Exercises.—In order to attain success with these exercises the patient must be made to understand that he is going to re-educate his limbs, that it is necessary for him to carry out the exercises as carefully as possible, to concentrate his mind on each movement and to try to store up all the impressions received while he correctly carried out the movements. It is often a help to him if the movements are first of all carried out passively, then actively with the eyes open and then actively with the eyes closed.

When the patient is unable to walk he must begin with bed exercises. Lying flat on his back he is trained to perform certain movements with his eyes open, such as placing his head in various holes or depressions in exercise boards which should be well padded to avoid injury. The boards are constructed to permit of lateral movements and antero-posterior movements. Later he can practise placing the heel of one foot on the knee, shin, ankle or toes of the other foot. The object of the exercises is to train him to perform accurately definite movements at first with the aid of vision and later with his eyes closed. The exercises should not be continued for too long at a time, five to ten minutes being ample at first; the duration depending upon the physical and mental state of the patient. They should be carried out four times daily and should always be supervised.

When these exercises are satisfactorily accomplished, exercises for the legs when seated upon a chair can be started, followed later by exercises when standing supported by hand rails. Later still with only one hand rail, and finally without support. The walking exercises are designed to train the patient to narrow the base, to place his feet within certain limits, to limit the length of the step and to enable him to walk upright. Later still he can be trained to walk toe and heel and to go up and down stairs.

In conclusion it is worth noting that every case benefits by the exercises and that in some the gait can be restored to normal. The most satisfactory cases are those who suffer from acute ataxia, and patients who suddenly become unable to walk may recover rapidly and be able to run or walk alone. In the slighter

cases of ataxia collective training under good supervision is often helpful owing to the stimulating influence of competition one with another. Hand exercises should be made as attractive as possible—placing cribbage-pegs, piano playing and typewriting being the most successful.

Trophic Changes

Perforating Ulcers.—In all severe cases, especially those in which there is much loss to pain and heat in the lumbar and sacral root areas, great care must be exercised to prevent the formation of trophic sores and ulcers. Socks and stockings should not have any irregularities such as darns at any place where they can exert pressure on the foot. The boots and shoes must fit well and patients should be warned against cutting their own corns, as this operation should only be performed by a skilled person with all antiseptic precautions. Should any ulcers develop they must be treated carefully and the patient made to rest until the sores have healed. Owing to the absence of pain, sores on the feet are apt to be neglected unless the patient is warned about them.

Arthropathies.—In the early stages the changes are confined to the soft parts, the ligaments becoming lax and the capsule of the joints distended with fluid. Judicious support with cotton-wool and a bandage or by elastic pressure may retard the progress of joint change. Bony changes must be dealt with on the same lines. Occasionally the enlargement of a joint may interfere with surrounding structures, such as nerves and blood-vessels, and necessitate surgical interference, but otherwise operation should not be undertaken. For the falling in of the arch of the foot a support on the inner side and broadening of the sole of the boot may be found effective, but great care must be taken not to produce any trophic lesion.

Sensory System

Pains.—The pains of tabes may be classified into three types—

1. Shooting pains which occur in paroxysms of varying intensity and duration; they are generally situated in fleshy parts of the limbs and not restricted to any special part, and are, as a rule, influenced by the weather. They can best be relieved by phenacetin, antipyrin, aspirin, or similar drugs. The action of these drugs is very individual, some patients being benefited by one much more than by the others. Morphia should not be given.

2. Pains of less intensity but greater persistence located to one part and commonly having a well-defined root distribution. These pains are at first associated with hyperæsthesia, but later with definite sensory loss. They may not be relieved by phenacetin or aspirin, but often yield to treatment with mercury and iodide. Some cases have been reported in which salvarsan has acted beneficially.

3. Pains of wide distribution affecting the skin and causing severe pain and hyperæsthesia which may persist for weeks. Local application of a liniment composed of equal parts of tincture of aconite, belladonna and chloroform, or of mesotan one part mixed with two parts of olive oil are sometimes serviceable. When phenacetin and aspirin fail to ease the pain aluminium chloride in two 4 gr. doses or ammonium chloride have been recommended as tending to reduce the severity of the pain, but as a rule anti-syphilitic treatment alone will procure any permanent relief. Morphia will ease the pain, but this should never be prescribed as the patients almost invariably develop the drug habit which remains long after the pains have ceased from troubling.

Crises

The treatment of the various forms of crises presents great difficulties and they often prove very intractable. Generally speaking, however, they tend to become less frequent and less severe as time goes on.

Laryngeal Crises are best treated by local application of a weak solution of cocaine or by a few inhalations of chloroform vapour.

Gastric Crises are the commonest of all forms of crises and when present often begin before the other symptoms and signs of tabes have become marked. For this reason many tabetics have been submitted to operation for appendicitis, gall-stones or renal colic. All patients who suffer from gastric crises should keep their bowels regular and avoid as far as possible any stomachic upset, for although the crises have no direct connection with the state of the stomach yet they may undoubtedly be set up reflexly by gastric trouble. Many remedies have been suggested and some succeed better than others in different cases. Drinking hot water, gastric sedatives such as bismuth with dilute hydrocyanic acid, and cerium oxalate sometimes relieve the vomiting. Small doses of belladonna, minim doses of tincture of iodine in water, or 7 gr. doses of chloretone may prove efficacious but often fail. Counter-irritation by means of hot water, a mustard leaf or galvanism may sometimes act beneficially, but they should not be used if there be much sensory change in the dorsal root areas. If these remedies fail then resource must be had to injection of morphia or codeia $\frac{1}{6}$ to $\frac{1}{4}$ of a grain.

Rectal Crises.—If the bowels be kept regularly opened the frequency and severity of the attacks will be diminished. In severe cases a

morphia suppository will be found most efficient.

GENERAL PARALYSIS OF THE INSANE

This disease is undoubtedly due to the action of syphilis and recently the spirochæte has been demonstrated in the brain and cerebro-spinal fluid of patients who have suffered from this disease.

Treatment.—Although the cause of the disease is well known anti-syphilitic treatment has up to the present signally failed in effecting its cure. Before the introduction of "606" some held that mercurial treatment was not advisable, although general opinion favoured its application on the ground that it did benefit early cases and might retard the progress of the disease. It remains to be seen whether salvarsan, neosalvarsan or intra-spinal injection of the blood serum of the patient after its reaction has been rendered negative will achieve any greater success. Some authorities have already condemned its use, while others claim for it substantial success; but in most cases little change has been noted in the condition of the patient. It seems clear, however, that if intrathecal injections are to be employed the dosage should be minimal. The injection of dead organisms such as streptococci and staphylococci has also been tried without much success. Ford Robertson has tried vaccine therapy, making use of the "Bacillus Paralyticans," but with little success.

General Management.—There can be no doubt as to the importance of early diagnosis of such cases, not only from the point of view of treatment but also for the sake of the patient and his relations. By means of the Wassermann reaction in the blood and cerebro-spinal fluid and by cytological and clinical examination of the cerebro-spinal fluid, the disease can be recognised in its earliest stages. When the diagnosis is made the relations should be warned as to the probable course of the disease and the possibilities which attend it — the danger of the patient ruining his social position by foolish or indecent behaviour, of dissipating his fortune or business by mismanagement or extravagant or insane schemes, and in some cases the possibility of attempts on his own life or on that of others. If the patient cannot be certified he should be sent away to the country under supervision, preferably in a home, and should there undergo active anti-syphilitic treatment. Rest, moderate exercise and freedom from business or other worries are essential, and indulgence in alcohol or sexual intercourse must be stopped. The reluctance which relatives express to having a patient certified is often due to the fact that they are not made fully aware of the risks to which they expose the patient and themselves by withholding their consent. If mental symptoms become obtrusive the patient should immediately be certified in order to secure adequate supervision and control. If the patient be dangerous care must be taken to see that he is provided with trustworthy and competent attendants.

Symptomatic Treatment

Congestive Attacks.—Patients are liable to attacks in which they may suffer from convulsive seizures, loss of consciousness followed by transient paresis and loss or impairment of speech from which they recover, but with a lowered mental state. These attacks are best treated by rest, sedatives, and keeping the bowels freely opened. If status epilepticus should develop chloroform may be necessary, or subcutaneous injections of amylene hydrate 5–10 per cent. solution may be used. If symptoms of cardiac failure appear saline infusions should be given along with inhalations of oxygen and stimulants such as caffeine or small doses of alcohol.

Irritability and Excitement.—For this, rest, quiet surroundings, and suitable companionship are necessary. A daily warm bath at a temperature of 86–90° F. or a continuous bath at 94° is useful in quieting the patient. Of drugs bromide and antifebrin in 5 gr. doses are the most suitable.

Feeding.—When the patient refuses food, resort must be had to nasal feeding every three to four hours, the food consisting of milk, to which may be added eggs or any drug which it is desired to administer. One to two pints may be given at a time.

The mouth should be kept clean as far as possible by means of swabbing with mild antiseptic lotion, and the bowels must be kept freely opened.

Later Stages.—As the disease progresses the patient becomes demented, paralytic and completely bedridden, unable to feed himself and absolutely indifferent to any sense of personal cleanliness. The treatment is confined to nursing; only continual care and attention will prevent the occurrence of bed-sores by insuring cleanliness and attending to the trophic condition of the body and limbs.

Juvenile General Paralysis or Juvenile Tabes.—Both these conditions may arise as the result of congenital syphilis or of early syphilitic infection. In view of this fact the offspring of every parent who has suffered from syphilis should be examined by clinical pathological methods for the presence of syphilis and, if the result is positive, should be actively treated.

T. G. S.

DISEASES OF THE BRAIN

TUMOURS

The medical treatment of intracranial tumours is confined, strictly speaking, to the treatment of symptoms, as surgery alone holds out any hope of cure or prolonged palliation. It is the physician, however, who seeing the cases in the early stages must treat the early symptoms, make the diagnosis and if possible localise the site of the tumour. Further, he may from his observations, be able to diagnose approximately the nature of the tumour, and so enable the surgeon to decide whether to make an osteoplastic opening or not.

Intracranial tumours affect the brain in two ways: (1) Directly—by local action, causing interference with the functions of, or actual destruction of, the nervous structures at or around the site of the tumour. (2) Indirectly—by causing a rise of the general intracranial pressure. The symptoms arising from this are headache, vomiting, optic neuritis, stupor, paralysis, coma and respiratory failure, and are known as the "general symptoms" of intracranial tumour. Cerebral surgery, although obtaining many brilliant results, has not so far fulfilled the expectations that have been hoped for. Surgeons complain that they are called in too late, and in many instances this is true. It is obvious that the sooner the tumour is removed or the pressure relieved, the less will the brain suffer from the direct and indirect effects of its growth, and further, should the tumour prove to be of a nature and in a situation which renders its removal possible, the earlier it is operated upon the less difficult is the surgeon's task and the less risk is the patient exposed to.

It may be that text-books of neurology have emphasised the general symptoms of intracranial tumour as being essential to the diagnosis, without due appreciation of the fact that the mode of onset of the symptoms may be quite as characteristic a diagnostic feature and quite sufficient in the absence of the "general symptoms" to warrant a diagnosis of intracranial growth.

It must be realised that the mode of onset and character of the symptoms depend upon three factors. The nature of the tumour, the rapidity of its growth and its situation. Thus, in some cases, local symptoms alone may be present for months or even years before the advent of general symptoms; in other cases local and general symptoms may develop contemporaneously, while yet again, in others the general symptoms may precede the local, and in some local signs may never appear at all. As the appreciation of these facts may have an important bearing upon the early diagnosis, the following table has been prepared, showing in a general manner the effect these factors exercise upon the development of the local and general symptoms.

Symptomatic Treatment. *Headache.*—Headache may occasionally be a localising symptom, in which case it is constant and always felt in the same spot, which may actually be tender on pressure, and is not amenable to medical treatment. Headache as a general symptom, however, is much more common. It is due to the increase in intracranial pressure and varies with it. Constipation, violent exercise, sudden changes of posture may excite it in the earlier stages, but later it becomes more constant. Persistent headache, especially in those who previously have been free from headaches, should always be regarded with suspicion, and ensure repeated, careful examinations of the patient, for other signs of intracranial growth. Treatment should be directed to lowering the intracranial pressure. The patient should rest in bed, the bowels should be freely opened and diuresis promoted. The most effective drugs for the relief of the headache are phenacetin, phenalgin, antipyrin, aspirin and allied substances in 5–10 gr. doses. A useful combination for such cases is a powder composed of 5 gr. each of phenacetin, caffein and aspirin.

Vomiting.—This also is a general symptom due to increase in intracranial pressure, and is commonly associated with headache. Its onset is sudden and unattended by nausea, and bears no relation to the taking of food. The treatment is essentially the same as that of the headache, namely, the lowering of the intracranial pressure.

Optic Neuritis.—This may develop early or late. Its onset may not be attended by any disturbance of vision, and its presence be unsuspected until detected by ophthalmoscopic examination. It is commonly associated with the other general symptoms, headache and vomiting, and should always be looked for in cases presenting these symptoms.

The only effectual treatment is decompression. It may happen that the position of the tumour has not been localised, and the question arises whether it is better to postpone operation in the hope that localising signs may appear and enable the surgeon to operate over the seat of the tumour, or to immediately proceed to perform decompression. If the case has been carefully watched and examined from time to time before the onset of the optic neuritis and no localising signs have been noted, there is no justification for delaying operation; but if such examination has not been made and the patient is suffering from signs of general pressure, it is advisable to attempt to lower

Nature of Tumour.	*Common seat of Tumour.*	*Local or Focal Signs of Tumour.* *Onset.*	*Character.*	*General Symptoms of Tumour.*
Bone.	Skull.	Late; develop slowly.	Local headache, fits.	Absent.
Neuroma. Neuro-fibroma. Fibro-sarcoma.	Attached to Trigeminal or acoustic cerebral nerves.	Early; develop slowly.	Local nerve palsies with later cerebellar and pontine signs.	May be absent or only arise late. When they commence are fulminating in character.
Fibroma. Fibro-sarcoma.	Dura—especially falx or orbital aspect.	Early or late; develop slowly.	Local headache, paralysis, mental change.	Appear late, are not acute; developing slowly.
Endothelioma.	Dura—falx or conversity.	Early or late; develop moderately rapidly.	Local headache, fits, paralysis, mental change.	Appear late, develop moderately rapidly but tend to be subacute for a long period.
Gumma.	Membranes or interstices of the sulci.	Early; developing rapidly.	Local headache, severe paroxysms, and associated with local tenderness, fits, paralysis, mental change.	Early or late; depending on co-existing conditions.
Hypophyseal.	Fossa Hypophyseos.	Early; of slow development, with co-existing glandular symptoms.	Headache, bitemporal hemianopia, or other ocular symptoms, optic atrophy.	Generally late and chronic; sometimes fulminating.
Glioma (A) Rapid (cellular).	Cerebrum.	Late if in silent area; otherwise early.	Paralysis, motor or sensory; mental change, fits.	Early; rapid and intense, may precede local signs.
	Cerebellum.	Early.	Nystagmus, vertigo, etc.	Early; rapid and intense.
(B) Slow.	Cerebrum.	Late; develop slowly.	Slight motor or sensory paralysis, fits.	May develop before local symptoms; chronic in type.
	Pons and medulla oblongata.	Early; develop slowly.	Cerebral nerve and pontine signs.	Absent or late in appearing, developing rapidly and fulminating.

the pressure, as in many cases this will reveal the presence of localising signs which have become masked by the rise of intracranial tension. This course can only be justified if it does not endanger the patient's life. Purging the patient and keeping him at rest may suffice, or lumbar puncture may be performed, but this is dangerous if there be signs of medullary compression. Should this plan be adopted the delay in operation must not be for long, and the vision must be tested daily, as any deterioration calls for immediate decompression. The question as to the best method of decompression does not fall within the scope of this article, but it may be stated that unless a large opening be made and the dura freely opened, no permanent benefit can be obtained. On the other hand, decompression may not only preserve vision, but even in cases where it has markedly deteriorated, result in complete or partial recovery.

Coma.—If a patient with cerebral tumour should suddenly become comatose, the administration of croton oil may restore him to consciousness and render surgical intervention possible. Lumbar puncture and the withdrawal of cerebro-spinal fluid may also be adopted as an urgency measure, but this is attended with a certain amount of danger, especially in cases with symptoms of respiratory failure. It may, however, be the only expedient possible.

Local or Focal Systems. *Fits.*—Intracranial growths may cause various forms of seizures.

Fits, localised or general, may arise from the direct or indirect effect of the tumour. Generally speaking, localised fits are due to the direct action of the growth, generalised to the indirect, but this rule is subject to many exceptions. If they occur early in the course of the disease they are more likely to be a direct result. In many cases it may not be possible to diagnose the cause of these seizures which may be due to idiopathic epilepsy—vascular or syphilitic disease. In favour of their being due to intracranial tumour are: (1) sudden onset late in life; (2) constant situation of the onset of the fits; (3) the development of permanent paralysis in the parts affected by the seizure; (4) the gradual onset of paralysis; (5) the development of general symptoms of intracranial tumour and the occurrence of headache and vomiting before the fits.

Treatment.—It may be advisable in order to localise the situation of a tumour, to postpone giving sedative treatment so that the character of the fits and the patient's subsequent condition may be observed. If the fits have been observed bromides should be given, the dose being adjusted to suit the requirements of each patient. If status epilepticus develops hyoscine $\frac{1}{100}-\frac{1}{50}$ gr. should be given, or chloroform inhalations resorted to. To withhold bromides in cases where a diagnosis has been made is bad practice, as a fit may cause hæmorrhage into the tumour, or death may ensue from cardiac failure subsequent to repeated attacks or from status epilepticus, which might have been prevented by the use of the drug.

Anti-Syphilitic Treatment.—When the nature of the tumour is doubtful a course of anti-syphilitic treatment has been recommended; this procedure is certainly inadvisable except in cases where the Wassermann reaction and the examination of the cerebro-spinal fluid indicate the presence of syphilitic nervous disease.

Even in cases of gumma, operation is often necessary to relieve pressure and save the patient's life. The cure of the condition, however, will depend upon subsequent active anti-syphilitic treatment, which often proves more effectual after operation than before.

Surgical Treatment.—There only remains to be considered under this heading, the question as to the best time for operation and the nature of the operation to be advised. For this purpose cases of intracranial tumour fall into two classes: (1) Those in which the situation of the tumour has not been localised. Operation should not be delayed when the patient has developed all the cardinal symptoms of intracranial tumour, provided the case has been under skilled observation, but if nothing is known as to the previous history, it may be worth while to endeavour to reduce the intracranial pressure by some temporary measure in order to reveal any localising symptoms. Immediate operation is indicated if the patient tends to become comatose, suffers from attacks of respiratory difficulty, or if there is progressive deterioration in vision. Neglect of the last point has resulted in many patients losing their sight. The choice of the seat of decompression must depend upon the conditions present in each individual case. (2) Those in which the tumour has been localised. In these cases operation should not be delayed, the skull should be opened over the seat of the tumour. If the history suggests the likelihood of the tumour being extra-cerebral a bone-flap may be made, but otherwise the bone should be freely removed. Should the tumour be extra-cerebral it should be removed when possible; if, on the other hand, the tumour be intra-cerebral, it is in most cases inadvisable to attempt to remove it. There are, however, cases where the tumour is cortical or subcortical, and where its boundaries can be plainly felt on palpation. If in these circumstances the growth is situated in a "silent" area, it is perhaps justifiable to excise it, but such cases are not common, and when there is any doubt as to the extent of the growth it is best to rest content with simple decompression.

Whether subsequent treatment by means of X-rays or radium can have any beneficial influence in such cases has not yet been demonstrated, and the application of such methods can only be regarded as experimental. The treatment of the paralysis must be carried out on the lines laid down in the section on the treatment of hemiplegia.

Abscess of the Brain

Brain abscess may arise from (1) disease of the ear; (2) disease of the accessory sinuses or of the skull; (3) injury; (4) bronchiectasis; (5) pyæmia.

In cases of disease of the ear the abscess may be extra-dural or situated in the temporal lobe or in the cerebellum.

The treatment consists of clearing out, as far as possible, the local ear disease, and if the abscess be extra-dural it can be drained through the operation wound. If the abscess is in the temporal lobe or in the cerebellum it must be opened up and drained, care being taken to prevent any spread of the infection.

In cases of disease of the accessory sinuses the primary form of infection should be explored and removed. The abscess is usually subdural or situated in the frontal lobe. The method employed for its evacuation must depend on the circumstances of each case.

Traumatic Abscess may be situated at the site of the injury or in some distal part.

Great care should be taken to render aseptic any wounds in the region of the head, but if an abscess has formed the skull should be opened over its presumed site and the abscess evacuated and drained.

In Pyæmic cases multiple abscess formation occurs, and little can be accomplished by surgical interference. If, however, there are definite localising signs and the patient's condition permits, operation should be performed.

In every case of cerebral abscess the patient should be given 10 gr. of urotropin thrice daily, as this drug is excreted into the cerebro-spinal fluid.

VASCULAR DISEASES

Disease of the cardio-vascular system may manifest itself in many ways, but never more strikingly than when it affects the function of the central nervous system. So much is this the case that it was customary to describe such conditions as cerebral hæmorrhage, cerebral thrombosis or cerebral embolism, as diseases of the brain. When looked at from a broader point of view, however, it becomes evident that the "disease" is confined to the cardio-vascular system, and that the brain symptoms are merely secondary complications due to vascular lesions which have damaged the cerebral structures. If this attitude be adopted the treatment of cerebral vascular lesions can be divided into preventive treatment (the treatment of the cardio-vascular disease), and the treatment of the cerebral lesion and its resulting paralysis. Cerebral lesions of vascular origin may be caused by a diminution or cutting off of the blood supply—as in cases of thrombosis or embolism—or by the rupture of an artery, as in cerebral hæmorrhage. In general terms the greater degrees of vascular disease, if associated with weak circulation or low blood pressure, favour the occurrence of thrombosis; if with a high blood pressure that of hæmorrhage.

Preventive Treatment.—Treatment of cardio-vascular disease. The cardio-vascular system must be considered from the point of view of the vessels and of the circulation.

Vessels.—Arterial disease may arise from many causes—syphilis, chronic renal disease, gout, chronic alcoholism, lead intoxication or senile changes. It may be a sequel to acute febrile diseases, and invariably results in cases in which there is a continued high blood pressure. Syphilis is the chief cause of vascular degeneration occurring before the age of forty; its action may be widespread or extremely local, and it may not be attended with any marked rise in blood pressure. In middle age syphilis, chronic renal disease, gout, chronic alcoholism, arterio-sclerosis and conditions of high blood pressure are the commonest causes, and the vascular changes are generally associated with high blood pressure. In old age atheroma and senile changes may be responsible, and vascular changes may be associated with a high blood pressure, but more frequently with circulatory enfeeblement.

Circulation and Blood Pressure.—The cardio-vascular system not only conveys blood to the body generally, but regulates the supply according to the functional requirements of the various organs. This adjustment of supply is brought about by dilatation and contraction of the arterioles and smaller arteries. If any organ requires a greater supply of blood the local vessels dilate while those in other portions of the body contract, and in this way maintain the normal blood pressure. Any disturbance in a system so extensive and complex reacts on the various organs of the body; the converse is equally true and the cardio-vascular system may be affected by disease of the various organs. It is well known that the internal secretion of various glands can influence the blood pressure, either by direct action, or through the vasomotor centres, and also that the blood pressure may be affected by the action of abnormal products arising from disordered metabolism.

It is obvious, therefore, that circulatory embarrassment and abnormal states of blood pressure may arise from an infinite variety of causes, and only by the most careful investigation of each case can the physician hope to remedy the defects. When treating a case of cardio-vascular disease his endeavour must be to maintain an efficient circulation, and at the same time to keep the blood pressure at such a level as will not cause rupture of the diseased vessels.

Cerebral Hæmorrhage

Before discussing the treatment of cerebral hæmorrhage, it is necessary to describe briefly the factors which underlie its production, and to review shortly the effect of cerebral hæmorrhage on the functions of the brain.

The occurrence of cerebral hæmorrhage depends upon two factors: (1) The state of the cerebral vessels, and (2) the blood pressure. Disease or weakening of the arterial walls is the primary cause in all cases, but the immediate and determining factor is a blood pressure sufficiently high to cause rupture of the damaged vessel. In most cases vascular disease is associated with an abnormally high blood pressure, but in others the blood pressure is little raised, the rupture being due to the excessive weakness of the vessel walls. This is specially apt to occur in cases of miliary

aneurysm or in persons who have previously suffered from cerebral thrombosis which has caused softening and further weakness of the vessel by depriving it of its outside support.

The Effects of Hæmorrhage on the Brain.—In addition to the local symptoms caused by the destruction of brain tissue, hæmorrhage causes a rise of intracranial pressure which is followed by (1) a rise in the general arterial pressure; (2) cerebral compression; (3) coma, and ultimately death from anæmia of the respiratory centres in the bulb.

Prophylactic Treatment.—Cerebral hæmorrhage can only be guarded against by treating appropriately the diseases or constitutional states responsible for the vascular changes and raised blood pressure. No practical physician can be blind to the dangers which threaten such cases and omit to protect his patient by advising him as to his mode of living without, however, alarming him by suggesting the imminence of a stroke.

General Hygiene.—A sedentary life should be avoided; the patient should be ordered a moderate amount of out-door exercise every day, avoiding sudden exertion or over-fatigue. Occupation is good, and it is a mistake to curtail the patient's work provided it does not entail excessive mental or physical strain. Meals should be taken regularly and leisurely. It is not possible to lay down any special dietary, as such must of necessity be chosen for each individual case, but above all it is important to avoid over-eating. Alcohol should be forbidden or limited, and if the patient be advanced in years, smoking should be restricted if not prohibited.

Treatment of the Stroke.—The patient must be kept absolutely still, and all unnecessary movement of the body forbidden. He should be placed in the horizontal position, with his head, neck and shoulders slightly raised, care being taken to see that the head is not flexed on the chest. All tight clothing should be cut away and the neck freed from any constriction. If the tongue falls back and obstructs his breathing the head should be slowly and gently turned so that the hemiplegic side rests on the pillow. Hot-water bottles well covered with flannel should be applied to the feet. If it be necessary to move the patient to hospital, this transference must be carried out as gently as possible, the head and shoulders being raised and supported. If the stroke occurs within doors, no attempt should be made to move him to his bedroom; when practicable a bed or mattress should be made up in the room in which the stroke has occurred, and in any case he should not be moved until everything has been prepared for his reception. In all cases of coma, a catheter should be passed in order to prevent distension of the bladder and to ascertain the condition of the urine.

The next problem is how to reduce the blood pressure. This may be effected by venesection or purgation. If the patient be moribund, or if there be any doubt as to whether the case is one of thrombosis or hæmorrhage, no active measures should be adopted. On the other hand, high arterial tension with a strongly acting and hypertrophied heart, calls for immediate action.

Venesection.—Some authorities object to venesection on the grounds that the cause of death is anæmia of the respiratory centres, and that to withdraw blood would aggravate the condition by lowering the arterial blood pressure. This objection is more theoretical than practical, and could only be upheld in cases where the hæmorrhage had ceased and the patient was in a state of coma. The anæmia of the respiratory centre, if present, is due to the rise of intracranial pressure secondary to the hæmorrhage, and the lowering of the intracranial pressure by venesection would more than compensate for the reduction of the arterial pressure. If venesection be decided on, a vein in the arm should be opened and 8–14 oz. of blood be removed.

Purgation.—At the present time purgation is more popular than venesection. If the patient be able to swallow, a cathartic pill or large dose of calomel can be given. In cases of coma the most efficacious method is to mix 1 or 2 min. of croton oil with 4 or 5 min. of olive oil and place them on the back of the patient's tongue. In all cases, whether purgation is desired or not, an enema should be given and the bowels kept freely opened.

Medicinal Treatment.—Unfortunately the action of most drugs which lower the blood pressure is very temporary, and is succeeded by a greater rise. There are very few drugs which have a permanent effect in lowering the blood pressure; the action of those which cause a rapid fall being very evanescent, and generally followed by a greater rise in pressure. If the patient can swallow and the blood pressure is very high, aconite may be tried. Five to ten min. of the tincture should be given as an initial dose, and this can be repeated at intervals of half an hour until the pressure falls 20–30 degrees or below 200 mm. If signs of poisoning develop—dilatation of the pupils, irregularity of the pulse, vomiting and a moist, cold skin—the administration of the drug must be stopped.

Sedative Treatment.—If the patient suffers from fits, delirium or restlessness, bromide and chloral should be given by mouth or per rectum. If these modes of administration are impracticable, hypodermic injections of hydrobromate of hyoscine $\frac{1}{100}$ gr. should be

tried. In some cases hiccough, retching and vomiting are most troublesome; this can be checked by hypodermic injection of $\frac{1}{6}$ gr. morphia sulphate combined with $\frac{1}{120}$ gr. atropine sulphate. Washing out the stomach has been recommended, but as the vomiting is usually of nervous origin, sedative treatment is preferable and less likely to disturb the patient.

Stage of Reaction.—If the patient survives the immediate effects of the stroke he passes into a stage of febrile reaction which may last for several days. During this time the temperature may be raised two to three degrees above normal, and rigidity be observed in the paralysed limbs. Constant attention and careful nursing is required, as hæmorrhage is liable to recur and bed-sores develop with great rapidity. A steady rise in temperature and the onset of Cheyne-Stokes respiration portend a fatal termination. On the other hand a fall of temperature and the return of consciousness, point to the patient's recovery. During this stage no stimulant should be given, and the bowels must be kept freely opened.

Stage of Recovery.—During the next few weeks the patient will recover slowly or rapidly according to the circumstances of each individual case, but before describing the treatment of the paralysis some details of the general management of the case should be considered.

The Sick-room must be well ventilated and an equable temperature maintained. Relatives should be discouraged from entering the room, and not more than one allowed in at a time, but the physician must use his discretion according to the circumstances of each case.

Prevention and Treatment of Bed-Sores.—Great care must be taken to prevent the development of bed-sores, the skin must be kept clean and dry by washing thoroughly, drying and powdering. Assiduous care and attention is necessary to prevent the skin round the genitals and buttocks from becoming sodden, and in this region the skin should be protected by ointment. Sores are specially liable to develop over the points of pressure. This may be averted by frequently changing the position of the patient should his condition permit, and by placing him upon a water-bed or easing the pressure by means of air-cushions or rings of cotton-wool; the bed must be kept free from creases, and the resistance of the skin can be increased by the daily application of a little spirit.

Feeding and Diet.—No attempt should be made to feed the patient by mouth during the first twenty-four or forty-eight hours. If his condition requires nourishment rectal feeding may be resorted to (see Article on *The Dietetic*

Factor in Treatment). When he is able to swallow he should first be fed with a spoon, great care being taken to prevent the passage of food into the lungs.

Diet.—During the first ten days his diet must be confined to milk, to which may be added egg or sugar. Six oz. may be given at a time at intervals of three to four hours. As the patient improves he may be given a more liberal diet, but all stimulating foods are to be avoided, red meat and articles rich in purin being prohibited.

Hemiplegia

Treatment of the Hemiplegia—The degree of recovery likely to occur cannot be foretold with any certainty during the early stages, as it depends partly upon the situation and partly upon the nature and severity of the lesion. In many cases the initial paralysis is due to disturbance of function rather than to actual destruction of the nervous tissues. No case should therefore be regarded as hopeless and unworthy of every possible effort to promote as complete a recovery as possible. The ultimate disability is due chiefly to (1) the degree of paralysis present; (2) spasticity; (3) adhesions in the joints, although in a small number of cases it may be due to sensory disturbances and affections of co-ordinating centres. It is undoubtedly the case that some patients who recover power of voluntary movement are unable to use their limbs properly on account of the spasticity and adhesions which have been allowed to develop.

Spasticity.—In order to prevent or diminish spasticity, treatment should be begun while the paralysed limbs are still flaccid. Passive movements should be carried out at all joints, and the muscles round the joint should be gently massaged. When spasticity begins to show itself the limbs must not be allowed to remain in any one position, and therefore in addition to the passive movements, the spastic contracture of the limbs must be combated by means of apparatus.

Upper Extremity.—The limb should be fixed for several hours daily or during the night in an extended position, abducted at the shoulder, extended at the elbow and hyper-extended at the wrist and finger joints. This is easily accomplished by placing the limb in light wire splints which have been adequately padded.

Lower Extremity.—The limbs should be kept extended, abducted with the foot dorsi-flexed at a right angle. The early application of such treatment will do much to prevent the spasticity; if, however, spasticity and contractures are already present they must be overcome by passive movements, hot-air baths and apparatus.

Should this not suffice tenotomies may have to be considered. Section of the posterior roots is not so applicable in cases of hemiplegia as in cases of diplegia, but may be used in selected cases.

Adhesions.—Early treatment with passive movements and massage round the joints will do much to prevent formation of adhesions. If, however, they are already present, they must be broken down by passive movements if necessary under an anæsthetic. The application of heat in the form of hot air or fomentations will diminish the pain and lessen the reaction. The local injection of fibrolysin has been claimed to have a favourable effect in controlling the subsequent formation of adhesions.

Treatment of the Paralysis.—The patient must be encouraged to make voluntary movements, and every increase in power or extent of movement should be pointed out to him by way of encouragement. Voluntary movement should be assisted by passive movements. As the power returns instruction must be given not only in making the movements but in executing them as correctly as possible; for this purpose cribbage-pegs and solitaire-boards may be utilised, also writing and drawing. Considerable difficulty may be experienced in those cases where recovery has been sufficient to permit the patient to get about and use his arm to a certain extent, his tendency being to perform the movements in what is to him the easiest way—thus in walking he will not attempt to flex the hip and bend the knee, but be content with circumducting his leg. If, however, he is trained from the beginning, and the necessity for practising the correct use of his limbs explained to him, he will soon realise for himself the importance of persevering with his exercises.

Subsequent Treatment of Cases of Cerebral Hæmorrhage.—What has been written above in regard to the prophylactic treatment of cerebral hæmorrhage may be taken as indicating the lines upon which the after-life of the patient must be arranged. Freedom from worry and anxiety and a quiet life in congenial surroundings is the ideal to be aimed at. The blood pressure must be carefully watched, and as far as possible maintained at a suitable level. Indulgence in alcohol and sexual intercourse should be prohibited, and smoking carefully regulated. The diet must be simple and non-stimulating, and the patient's bowels must be kept open regularly. Above all, the patient should not be depressed by having the threat of an impending stroke held over him, rather should he be encouraged to regard the first stroke simply as a warning that he must curtail his mode of life to meet the requirements of his physical state.

Cerebral Embolism

The commonest cause of cerebral embolism is endocarditis. The embolus may also result from the detachment of a portion of an intracardiac clot or of a thrombus formed in any portion of the circulatory system which conveys the blood from the heart to the brain. In septic cases the emboli are usually multiple.

Treatment.—Cerebral embolism must be regarded as a complication of any of the above conditions, and every precaution must be taken to prevent its recurrence. The patient must be kept absolutely at rest, stimulants should not be given unless his general condition necessitates their administration. If the heart be acting too strongly, sedatives should be employed, but in most cases rest is all that is required. If the patient be very restless morphia should be given. Apart from this the treatment and management that is essential is similar to that employed in cases of cerebral thrombosis.

Subsequent Treatment.—For the treatment of the hemiplegia, the reader is referred to the treatment of *Hemiplegia* under Cerebral Hæmorrhage.

Cerebral Thrombosis

The factors predisposing to cerebral thrombosis are: (1) Vascular degeneration (syphilitic or atheromatous); (2) circulatory enfeeblement (cardiac or general); (3) combination of the above; (4) abnormal blood states; (5) tumours, gummata or abscess, which by pressing upon vessels obstruct the flow of blood.

Treatment.—The general treatment of the stroke and subsequent paralysis is the same as that described for cerebral hæmorrhage. The special treatment of each case depends upon the cause of the thrombosis.

Treatment of Thrombosis due to Vascular Disease. 1. *Syphilitic Vascular Disease.*—Syphilis is the commonest cause of vascular disease before the age of forty, and it may cause thrombosis quite apart from any circulatory disease. The extent of the syphilitic vascular disease may vary in extent and degree, in some cases being widespread, in others peculiarly local. It may be associated with obvious syphilitic or para-syphilitic nervous disease. In all cases the patient should be put to bed and the bowels well opened. Active treatment by inunction with mercury should be carried out at once and at the same time large doses of iodide should be given. Salvarsan or neosalvarsan should not be given immediately, but may be employed safely three weeks after the onset of the stroke. Stimulants are not indicated unless there is profound circulatory

enfeeblement, a condition which is rarely met with in such cases.

2. *Arterio-Sclerosis Associated with Renal Disease.*—Speaking generally, such cases suffer from hæmorrhage rather than from thrombosis, but thrombosis occurs more frequently than is recognised. It is met with usually in cases where compensation is failing, or where there is a temporary enfeeblement of circulation due to some acute condition such as influenza. In such cases rest is all that is required, supplemented, if need be, by some cardiac stimulant, but in most cases rest alone will relieve the circulatory enfeeblement. It must always be borne in mind that thrombosis still further weakens the vessel by depriving it of the support of the surrounding tissues and that such a vessel is ill-fitted to resist the strain of a hypertrophied heart and raised blood pressure. When the patient recovers from the thrombosis steps must be taken to prevent the blood pressure from rising to a dangerous level.

3. *Senile Arterial Changes.*—In these cases rest is essential, only mild aperients should be given and warmth should be applied to the feet. Cardiac stimulants should not be given in cases in which there is the history of previous thrombotic attacks or where there is evidence of cardiac hypertrophy, unless the cardiac condition makes their use imperative. Diffusable stimulants may be given as a temporary measure; where there is chronic cardiac weakness iron and arsenic will be found most useful, together with plenty of rest.

Treatment of Thrombosis due to Circulatory Enfeeblement.—Such cases are extremely rare and can only be prevented or treated along the lines essential for the treatment of the cardiac trouble, whether arising from acute or chronic cardiac disease or general debility. Rest and stimulants are required in most cases.

Treatment of Thrombosis due to Combination of the above causes.—In many cases although cardiac enfeeblement may be the predominant cause of the thrombosis, vascular changes of varying intensity are associated with it. The giving of stimulants must be determined by the circumstances present in each individual case, stimulation being given in inverse proportion to the degree of vascular change present.

Treatment of Thrombosis due to Abnormal Blood States.—Thrombosis may occur in cases of pernicious anæmia, leukæmia, chlorosis; it may also develop as the result of changes in the blood and circulation. In pregnancy, typhoid fever, tuberculosis, diabetes, septicæmia and pyæmia. The treatment of all such cases is essentially that of the causal condition.

Treatment of Thrombosis due to Local Obstruction by Pressure from without.—In a few cases thrombosis may arise as the result of pressure exerted upon a vessel by tumour, abscess or chronic inflammatory changes. As a rule evidence of the obstructing cause is present for some considerable time before the onset of thrombosis, and should be appropriately treated by medicinal or surgical means.

Subsequent Treatment of Cerebral Thrombosis.—Syphilitic cases should receive routine treatment with mercury and iodide, and should be encouraged to make the best use of their limbs. In the other forms avoidance of fatigue, excitement or over-work should be insisted upon, but the patient's life should be made as bright as possible. General tonic treatment is indicated, care being taken to regulate the blood pressure according to the necessities of each case.

T. G. S.

CEREBRAL AND CEREBELLAR PALSIES OF INFANCY

Cerebral Palsies. (*Cerebral Diplegia*).—Before undertaking the treatment of a case of cerebral diplegia, it is important to recognise the nature and the cause of the affection, whether the condition is due to (i) defective development of the cerebrum or cerebellum, (ii) a progressive cerebral degeneration, (iii) some injury or inflammatory lesion, either natal or pre-natal. The defect in development may be so great as to amount to a complete agenesis of the cerebral hemispheres; the basal ganglia, pons, cerebellum, medulla and spinal medulla being normally developed. Such a case calls for much attention, but little treatment.

In those cases in which a condition of progressive diplegia is present, some toxic agent such as syphilis must be thought of, and the condition known as juvenile general paralysis, due to congenital syphilis, gives rise to a progressive spastic paraplegia. A tumour of the pons will also give rise to symptoms of spastic paraplegia. Cases of cerebral diplegia, which are dependent on some passed lesion, which is not progressive, are those most suitable for treatment, and it is the spastic condition of the lower limbs which calls for special treatment. The spastic condition of the limbs is in the slighter cases relieved by passive and active movements of the legs, by massage and by the application of heat in the form of baths. In the slighter cases such a line of treatment suffices to keep the limbs free from marked hypertonia. In some cases tenotomy may have to be performed to overcome the contraction of the tendons which has taken place.

In the severer cases the spastic condition cannot be overcome by such methods, and it has been suggested by Foerster that the posterior roots of the spinal medulla should be cut so as to

abolish or diminish the tone of the muscles. The roots which are selected for this purpose are the second and third lumbar, the fifth lumbar, and second sacral. Not more than two consecutive roots should be cut, and that which supplies sensation to the sole of the foot (viz. sacral 1) should, if possible, be left intact. The operation of dividing the obturator nerves in cases of marked adductor spasms has been advocated, but the operation has not as yet had an extended trial.

It is important to continue the treatment by massage, exercise and splints after section of the roots. Mechanical support will, in some cases, greatly help the patient to get about, but it is essential by the careful performance of tenotomies to get the limb in a good position before instruments are applied.

Cerebellar Diplegia.—The characteristic symptom of this affection is ataxia, and it is to this symptom that attention is directed in dealing with these cases. The ataxia affects the head, limbs and trunk. Co-ordinated exercises both for the legs and hands should be given. A cribbage or solitaire board is useful for educating the movements of the hand. For walking, a "walking apparatus" should at first be used followed by toe, heel and footstep exercises. It is needless to say that massage, passive and active movements, often greatly help these children.

In the hypotonic forms of cerebral diplegia in which there is marked mobility of the limbs, some improvement will take place with careful training, massage and suitable splints. The celluloid splint is most suitable for this class of case.

Hereditary Cerebellar Ataxia.—This disease is characterised by ataxia, associated with optic atrophy. It is usually slowly progressive, and no treatment is known that can arrest the disease. The ataxia may be improved by co-ordinated exercises, massage and general hygienic attention, but no permanent arrest of the disease can be expected.

Friedreich's Ataxia.—This disease, which commonly affects several members of a family, begins at an earlier age than the above, and manifests itself during the first decade of life. The chief symptom, viz., ataxia, may be treated by co-ordinated exercises and movements; but the disease is generally slowly progressive and leads to complete incapacity during the second or third decade of life.

Family Amaurotic Idiocy.—This disease occurs chiefly in Jewish children during the first or second year of life, males and females and successive members of a family being alike affected. It is a slowly progressive cerebral degeneration, attended by loss of mental faculties, loss of motor power and blindness, with a characteristic red spot in the centre of the macula. A form of this disease also occurs in late infancy and the juvenile period of life, attended by the same symptoms but without the characteristic macula changes, and without the special race disposition. The cause of this condition is certainly not syphilis, but the nature of the toxin is unknown. No treatment has hitherto been effectual in arresting the disease.

F. E. B.

APHASIA AND APRAXIA

The treatment of aphasia and apraxia depends on several factors, of importance also from a prognostic standpoint. Reference will first of all be made to these.

It has often been maintained that the older the patient the less likely is recovery of speech to ensue. This is far, however, from being the case. In the writer's experience it is peculiarly difficult to say in any given case what the outlook really is. Although the patient is well on in years spontaneous improvement may set in. As a general rule, those cases will make a fair recovery where the interval between the "stroke" and the reawakening of speech is short. It has been held that sensory aphasia is less likely to be recovered from than motor aphasia, but I have not been able to convince myself of the truth of this statement. On the severity of the attack much will depend. In a large number of cases the aphasia may be described as transient, as, for instance, in Jacksonian epilepsy, in migraine, in arteriospasm, in certain toxic and toxi-infective conditions, such as encephalitis, enteric fever, smallpox, measles, and poisoning by such drugs as belladonna, cannabis indica, opium, as well as in snake-bite, and so on. But where an aphasia is definitely established, in an elderly individual, prognosis should always be guarded. If there is little indication of generalised disease of the circulatory or renal systems the outlook is better than if these systems are grossly affected. If the aphasia is not complicated by concurrent paralytic phenomena the situation is, as a rule, more favourable than if these are present. But to this general rule there are, unfortunately, discouraging exceptions. The larger the lesion, the less certain is improvement to occur. In some cases functional restitution takes place, *i. e.* the actual lesion undergoes diminution, so that parts of the brain that have been damaged resume functional activity. In some, functional compensation may be expected, *i. e.* auxiliary speech mechanisms develop in undamaged parts of the cerebral cortex.

In all cases of aphasia, treatment is conducted along two lines : (1) the treatment of the actual diseased condition, and (2) the treatment

of the symptomatic aphasia, once it is established and more or less stationary.

The commonest causes of aphasia are embolism, hæmorrhage, thrombosis, inflammations, and tumours. The special treatment of these varying conditions is described elsewhere, and will not here be referred to.

Treatment directed to the restoration of speech by functional compensation or restitution is what here concerns us. Notwithstanding differences of opinion, it is the writer's experience that re-education methods will repay, and that even a partial return of speech is worth striving for. Pedagogic methods now in vogue are the following: repetition methods, in which the patient is made to repeat exclamatory monosyllables, such as "ah" or "oh"; then monosyllabic nouns or pronouns: then verbs, polysyllabic nouns, and so on. Each time a noun is named, the patient is shown the object, and allowed to handle it, and at the same time its name is written or printed on a piece of paper before him. He is made to repeat the letters of the alphabet, the letters being held in front of him, and similarly with the numerals from one to ten. It is plain that the method is one capable of wide modification and expansion to suit particular cases. Phonetic methods, such as that advocated by Wyllie, consist in the patient being made to master the letter-sounds; he is shown by direct lip-reading how to place the lips, tongue, etc., for the pronunciation of each letter-sound. Goldscheider commences with the simplest vowels and the explosives, and gets the patient to articulate Pa, Pe, Po, then Ba, Be, Bo, and so on. The consonants N, F, W, etc., are utilised after the same fashion. These and similar methods, it will be seen, are based upon the processes by which a child first learns the elements of speech, the details being varied according to the individual. Excellent results have been obtained even in what have at first appeared to be disheartening cases.

Hitherto reference has been made mainly to cases of motor aphasia, but the principle of the methods is applicable also to sensory aphasia. In cases of word-blindness, for instance, the patient must be treated as a child learning to read for the first time, especially if he is letter-blind as well as word-blind. It need scarcely be said that if the best results are to be attained, there must be diligence on the part of the patient, with enthusiasm and patience on the part of the teacher.

By apraxia or dyspraxia is signified the inability to perform certain movements or series of movements in the absence of any motor or sensory paralysis or ataxia. The patient cannot perform certain movements voluntarily, although he may innervate the same muscular mechanism involuntarily. Apraxia may be either unilateral or bilateral. Motor apraxia closely resembles motor aphasia: apraxia has been termed "aphasia of the arm." The commonest causes of apraxia are cerebral vascular lesions and tumours, especially of the corpus callosum and posterior parts of the frontal lobes. It also occurs in certain mental diseases, outside the scope of this article. On the analogy of what has been already said in regard to motor aphasia, the treatment of the apraxic must consist in the slow and laborious retraining of the limb for such acts as are lost or defective. Agraphia is a variety of apraxia, and should be treated along the lines already sufficiently indicated. If the right hand is out of action from a "stroke," the patient must be taught assiduously and laboriously to use the left hand. Sometimes the results are surprisingly good: often graphic power is rapidly acquired. If the right hand is available, it is an excellent plan to train the patient in the simultaneous employment of both hands in performing simple writing exercises, such as letters, geometrical figures, etc.

S. A. K. W.

HYDROCEPHALUS

Internal hydrocephalus is a condition which may be either acute or chronic. It may be the sequel to subtentorial lesions (growths, abscesses, cysts, caseous formations) so placed as to interfere with the circulation of the cerebro-spinal fluid through the iter, or it may be associated with meningeal or vascular conditions (serous, tuberculous or suppurative meningitis, epidemic cerebrospinal meningitis, ependymitis, sinus thrombosis). Treatment should, therefore, where practicable, be directed to the underlying condition. Congenital hydrocephalus is a type which is noticed at birth and is frequently associated with malformations of the brain; it is highly doubtful whether hydrocephalus can ever be described, in the strict sense, as idiopathic.

The symptomatic treatment of hydrocephalus may be (1) medical, on the assumption that the condition is associated with congenital syphilis, but it is doubtful whether treatment, *e. g.* with mercurials, is efficacious. (2) Lumbar or cranial puncture is often resorted to. It is clear that only certain types of hydrocephalus can be benefited thereby, and puncture must be repeated again and again. At best such procedures are unsatisfactory. (3) Surgical treatment by various drainage devices has sometimes been successful. One of the best methods is to pass a silk drain from one or other lateral ventricle into the subcutaneous tissues of the neck. Cushing recommends

peritoneal drainage from the spinal theca. Some cases where the posterior roof of the fourth ventricle has been freely incised and drainage established have been followed by good results.

S. A. K. W.

BULBAR PALSY

1. The progressive type of the disease is identical with progressive muscular atrophy, *q. v.*

2. Bulbar palsy of acute onset may occur due to thrombosis of the basilar artery or its branches. In such cases during the acute stage, the patient should be kept as quiet as possible, in bed, and treated symptomatically, drugs, such as strychnine, atropine and alcohol being used as necessary. Should the patient survive the acute attack, and evidence of syphilis be forthcoming, antispecific treatment should be energetically administered, (neosalvarsan, mercurial inunction, iodides). Feeding must be very carefully carried out, semi-solids being swallowed most easily, but feeding by tube may be necessary for a time.

3. Bulbar palsy of acute onset may also occur as the result of polioencephalitis. In this condition the treatment is purely symptomatic, every effort being made to keep the patient alive till the inflammatory condition has subsided.

4. Bulbar palsy may result from double hemiplegia, *q. v.*

5. Bulbar palsy may result from lesions, such as gummata or new growth involving the vagus, accessory and hypoglossal nerves at the base of the skull. The former are susceptible of treatment by antisyphilitic remedies, and therefore every effort should be made to establish the diagnosis in such cases.

C. M. H. H.

DISEASES WITH INVOLUNTARY MOVEMENTS (OR TREMORS)

Chorea

For the purposes of this article chorea is taken to mean the ordinary Sydenham's chorea of children. Huntington's chorea is discussed elsewhere, also chorea gravidarum.

Sydenham's chorea is in all probability always a manifestation of rheumatism, although as a rule, even when the case is acute, there is little or no rise of temperature. In acute cases the child must always be put to bed, and, whether at home or in hospital, it is very advantageous to surround the bed with a screen. Dejerine's epigrammatic rule is worth remembering: "Au lait et au lit." Not a few cases recover without further treatment than rest in bed. If the movements are, as they may be, literally such as to jerk the child out of bed, restraint by bandages, or by binders over the bedclothes, may be called for. In mild cases rest in bed must still form part of the treatment: the child should at any rate go to bed early and get up late. It is very common indeed, in the writer's experience, to find that cases where the movements are so slight that a "change" to the country, to a convalescent home or otherwise, has been recommended, return with an aggravation of the symptoms. There has been no rest, or it has been inadequate.

But although some cases recover without medicinal aid, it is more satisfactory to utilise certain drugs at our disposal. Of these undoubtedly the most efficacious is aspirin. It is practically a specific in this affection. Ten or fifteen grains should be given four times in twenty-four hours, or oftener, to begin with. After a week the dosage may be reduced if the case is progressing favourably. Liquor arsenicalis has long held pride of place in chorea, but it is not so useful as aspirin, and it presents obvious disadvantages. It is frequently given in small doses, ♏ i or ii, increasing at regular intervals to ♏ x or even more. As a rule it is tolerated unexpectedly well by children. Very many sedatives—*e. g.* the bromides, trional, chloral hydrate, chloretone, chloralamide, antipyrine, hyoscyamus—have been tried at one time or another; the anti-rheumatic remedies, however, are for general purposes sufficient. Acute chorea, rebellious to these, has been successfully treated by small doses of apomorphine, gr. $\frac{1}{30}$ to begin with, which may be increased, and this should be noted for those cases where the movements are violent and the exhaustion extreme. In addition to apomorphine, the best drugs for the really violent cases are choral hydrate (beginning with, say gr. iii), or syrup of chloral hydrate (beginning with ♏ xx), chloralamide (gr. x or more), hyoscine hydrobromide gr. $\frac{1}{200}$ or less) cautiously given. In desperate cases a whiff of chloroform at brief intervals may have to be resorted to. As the child is convalescing, cod-liver oil with maltine is a favourite tonic.

Massage is of service as the movements are coming to an end. Often a curious abruptness of movement remains though the irritative phenomena have ceased; sometimes, again, the movements, or rather some of the movements, persist as a sort of tic—a condition very closely allied to the "variable chorea" of Brissaud. In these cases exercises for the limbs are of great value.

In moderate cases the diet must be fluid and nourishing: milk, milk foods, eggs, soups, beef tea, meat extracts, are all to be recommended. In the bad cases it is perhaps advisable to omit extractives. A lacto-vegetarian régime is best during convalesence; meat as a rule is too

stimulating. Sometimes the adequate feeding of the patient is a difficulty, and nasal feeding must be resorted to. Often the feeding of a choreic child calls for a great deal of patience on the part of the nurse.

It is the chronic cases of chorea that are the most unsatisfactory. The physician must in the first place make sure that the movements have not degenerated into a tic, as noted above. Tics are treated along special lines. If he is dealing merely with recurring attacks of chorea, so frequent as to merit the term "chronic," it is advisable to institute a rigorous course of antirheumatic treatment and to consider the question of removing the child to a place where rheumatism is rarely met with. Hydrotherapeutic treatment is of value in such cases.

Paralysis Agitans

If the exact nature of the pathological process underlying paralysis agitans is still *sub judice*, no one doubts that the disease is essentially an organic degenerative disease of the nervous system, and the problem of its localisation, if not actually solved, is certainly less mysterious than it was formerly considered to be. After vascular and other lesions situated in the subthalamic region and in the mid-brain, tremor may develop which is for all practical purposes identical with what is seen in that disease; after certain hemiplegias tremor and spasticity may arise so similar to what obtain in that affection that the clinical picture is indistinguishable from a unilateral paralysis agitans, and it is well recognised that in the disease a unilateral commencement is far from uncommon. Progressive lenticular degeneration, a nervous disease in which the lesion consists of a bilateral degeneration of the corpus striatum, in particular the lenticular nucleus—which has intimate anatomical relations with the regio subthalamica and the nucleus ruber of the midbrain—has among its prominent symptoms a combination of tremor and of spasticity (the pyramidal paths being intact) which very closely resemble those of paralysis agitans. Not a few cases of double hemiplegia present striking analogies, from the clinical standpoint, to the symptom-complex of the disease under consideration. It may therefore be said, speaking generally, that paralysis agitans is a nervous disease occasioned by a degeneration in function of certain collections of grey matter and certain correlated nerve paths in the region already specified, associated no doubt with a structural change the precise nature of which is at present unrecognised.

This being so, it will readily be appreciated that the treatment of the affection has not passed the empirical stage. Attention should be directed to (1) the tremors, (2) the stiffness and weakness, (3) the general treatment of the patient.

Among the most satisfactory drugs in controlling the tremors are hyoscine or scopolamine. The hydrobromate of hyoscine may be given in doses of $\frac{1}{200}$ gr. twice or three times a day, combined with sodium bromide, and increasing to $\frac{1}{100}$ or $\frac{1}{60}$ gr. Scopolamine hydrobromide from the therapeutic standpoint is practically the same drug. Hyoscyamine sulphate gr. $\frac{1}{200}$ three times a day, may be given a trial. Tincture of hyoscyamus can also be recommended, in doses of $\frac{1}{2}$ to 1 dr. Many other sedatives have been tried.

For the stiffness and weakness light massage, coupled with passive movements, may be recommended. Exercises calculated to develop weak muscular groups and to counteract flexion attitudes may be resorted to, at least in the early stages, but they should be utilised with discretion, and should never be allowed to fatigue the patient.

Warm baths followed by a good rub-down are often helpful. While electricity in one or other form has often been tried, its effects are problematical; nevertheless I have had distinctly encouraging results by the prolonged use of high frequency to the back and limbs. For general purposes extract of parathyreoid gland has been vaunted, and may be tried in small doses. Pituitary extract is also worthy of a trial. Ordinary tonics of the strychnine type simply aggravate the condition.

Huntington's Chorea

Huntington's chorea is essentially a degenerative condition, progressing ultimately to dementia, in which the pathological substratum consists of chronic miliary encephalitic or meningo-encephalitic changes in the cerebrum. The exact nature of the pathological change, and its exact correlation with the clinical symptoms, are still uncertain.

No drug is known to exert any influence on the progression of the malady, which is in many cases hereditary. Arsenic has been tried, without encouraging results. The prolonged exhibition of urotropin, 10 gr. three times a day, is worth a trial.

Tetany

Much evidence has accumulated which goes to show that tetany, which is the name given to recurrent attacks of painful spasms or cramps in various muscular groups, especially those of the periphery of the limbs, is toxic or toxi-infective in origin; its occurrence is certainly associated with widely differing factors. It is common in rickets, during or after infective diseases such as cholera, typhoid, etc., in gastro-

intestinal disturbances, specially gastric dilatation, after total removal of the thyreoid, being apparently in this case the sequel to extirpation of the parathyreoids, etc. Of 528 cases in Austria, collected by Frankl-Hochwart, 223 were in shoemakers and 117 in tailors; possibly some toxin in the materials handled predisposes to the condition.

Treatment obviously should be both symptomatic and directed to the primary cause, where such is discernible. The severity of the painful spasms or cramps may be lessened by resort to bromides, chloral or some preparation of opium. A pill of zinc valerianate 1 gr. and extract of cannabis indica $\frac{1}{4}$ or $\frac{1}{6}$ gr. can be recommended for its sedative action.

Special attention should be given to the condition of the alimentary canal, and suitable treatment adopted for any pathological defect in function. If rachitis is a factor it must be treated accordingly. Extract of parathyreoid gland will be useful where there is reason to suppose the parathyreoids are impaired.

Idiopathic Tremor

Tremor is a symptom which may or may not be associated with a demonstrable organic lesion. Tremor is prone to occur in lesions of the corpus striatum, nucleus ruber, tegmentum and mid-brain generally, and where the rubrospinal path is impaired in function; it occurs in such known conditions as paralysis agitans, disseminated sclerosis, etc.; in hysteria it is often met with; in chronic intoxications as with lead, mercury and so on. Senile tremor and familial tremor are conditions whose underlying pathological basis is not fully understood. In every case effort should be made to get at the determining cause of the tremor, and where this is attainable it should be treated. For obscure and idiopathic cases of tremor sedatives such as scopolamine, hyoscyamus, the bromides, hydrobromic acid, may be given a trial, but they are unlikely to prove of much value.

Paramyoclonus Multiplex

Myoclonus is a symptom, consisting in sudden abrupt shock-like contractions of a muscle or muscular group, and it occurs in a multiplicity of pathological conditions. Of great practical importance it is to remember that myoclonus is very common in epilepsy—much more so than is usually supposed—and it may even occur as a true epileptic equivalent. Appropriate treatment is indicated in such a case. Myoclonus may be of the nature of a tic (*q.v.*). It may also be a hysterical phenomenon, and should be treated in such a case by appropriate measures. Paramyoclonus multiplex is the name given to a supposed morbid entity characterised by "violent clonic spasmodic contractions of muscles or muscular groups usually symmetrically situated, without other disturbance of motor or sensory function." Electric treatment has often been of value, at least for a time. So-called central galvanisation may be recommended, the electrodes being at the upper and lower extremities of the spinal column. Static treatment (static baths, breeze, sparks, etc.) have been found serviceable. Any nerve sedative or hypnotic may be utilised. General treatment along hydrotherapeutic lines meets with some success. Recently intramuscular injections of sodium cacodylate (1 to 2 gr.) have been recommended.

Post-Hemiplegic Involuntary Movements

These, when they occur, are practically always of the nature of hemi-chorea, hemi-athetosis, or hemi-tremor. Post-hemiplegic movements have been shown to make their appearance only when there is evidence that certain areas of grey matter in the basal ganglia, subthalamic region or mid-brain are implicated along with the pyramidal fibres themselves. Further, for their occurrence it is essential that the pyramidal paths should not be too severely injured; if and as long as there is absolute paralysis, no involuntary movements of the above-mentioned types will be found. It is important to note these facts, for it will thus be the more readily understood that post-hemiplegic involuntary movements are an indication of the extent of the lesion and of subsequent degeneration, and at the same time it will be realised how prone the condition is to be intractable. As a matter of fact, little can be done in such cases. Sedative treatment with the usual drugs is unavailing. (For general treatment, see *Hemiplegia*.)

Athetosis

Athetosis is an involuntary movement or movements of a limb or limbs, consisting in a sinuous, slow contraction and relaxation of certain muscular groups, sometimes culminating in a transient immobilisation of the limb in a spastic attitude. It may occur as a sequel to a hemiplegia (see *Post-Hemiplegic Movements*) or it may be bilateral and coupled with spasticity—so-called double athetosis, a condition allied to cerebral diplegia.

In the strict sense the condition is unalterable and incurable; cases of double athetosis may live a long life with no discernible modification of the symptoms during it. Some cases have been described (by Brissaud, Spiller and others) where treatment by nerve transplantation, nerve anastomosis, or resection of selected posterior spinal roots has resulted in a diminution of the involuntary movements and of the mobile

spasm. The benefit accruing from these surgical procedures has been to a certain extent encouraging.

Progressive Lenticular Degeneration (Syn. *Tetanoid Chorea*)

Progressive lenticular degeneration is a nervous disease, not infrequently of a familial type, in which bilateral degeneration of the lenticular nucleus, associated—as it constantly is in this affection—with cirrhosis of the liver, produces a symptom-complex of bilateral tremors, spasticity, emotionalism, dysarthria, dysphagia, contractures, without any clear indication of involvement of the pyramidal tracts, *i. e.* without ankle clonus or extensor response. In view of the fact that the disease is rare and that, while its pathology is very definite, its etiology and exact nature are still undetermined, treatment must be symptomatic and empirical. There is every reason to suppose that the disease is toxic in origin, and in the cases which I have had under my own care I have tried urotropin over long periods because of its recognised value in cases where the cerebro-spinal fluid is known to be toxic. I cannot say, however, that any obvious improvement took place. Until more knowledge enlightens us, the treatment of progressive lenticular degeneration must remain unsatisfactory.

Torticollis

Under the term "torticollis" are included various conditions which differ widely in their pathogenesis, if not also in their pathology, although this is a subject greatly in need of elucidation. The physician should not be content with diagnosing torticollis—a condition, needless to say, which is recognisable at sight—but should in each instance endeavour to ascertain the type of torticollis with which he is dealing, otherwise treatment is prone to remain unsatisfactory.

1. **Neuralgic Torticollis.**—Corresponding to the tics and spasms of the face that accompany facial neuralgia (tic douloureux), are the spasmodic torticollic movements that accompany occipital neuralgia. The torticollis in this case is usually tonic, but may be clonic. With the cessation of the neuralgic pain the twitching and stiffness of the neck muscles disappear. In these cases treatment should primarily be directed to the condition of occipital neuralgia, and should be conducted along approved lines.

2. **Professional Torticollis.**—This variety is essentially an occupation neurosis, analogous to writer's cramp. It occurs only at the moment of execution of a given act which implicates the muscles of the neck; at other times the movements of the neck are normal. A combination, indeed, of writer's cramp and torticollis is not uncommon. According to Cruchet, tailors, cobblers and pavers are liable to this form of occupation neurosis; it occurs also in seamstresses and in hat-makers, according to my own observations. It should be treated along lines suitable for occupation neuroses.

3. **Paralytic Torticollis.**—This is a little-recognised condition, in which a spasm develops in the neck muscles similar to the secondary facial spasm following a facial palsy. The spasm is apt to pass on into the next type, as are also, in some cases, the conditions described under (1) and (2).

4. **True Spasmodic Torticollis.**—Idiopathic spasmodic torticollis is familiar. The movements are tonic, clonic or tonico-clonic; certain muscles are rigid, and some pain accompanies this rigidity. The influence of the will on this condition is practically nil; and it is usually impossible to correct the spasm by holding the head with the hands. It is a hemispasm of the neck analogous to facial hemispasm. This variety may also occur symptomatically in the course of such diseases as malaria, influenza, rheumatism, etc. It may be treated by a sedative galvanic current, the anode being used as the active electrode and a current of 5 ma. given. Both sternomastoids and both groups of posterior rotators may be treated in this way with advantage. Suspension, an old form of treatment, has been, in some cases personally observed, followed by a very good result. Massage is not of any special value, but resistive movements calculated to strengthen the muscular groups not involved in the spasm may be recommended. Rest in bed and immobilisation by means of sandbags, etc., placed at the sides of the head is not a method that has proved of much value. Possibly treatment by alcohol injections, as for facial spasm, might be worth trying in inveterate cases, but as far as I know no cases treated in this fashion have as yet been recorded. It is in this true spasmodic torticollis that surgical interference may not infrequently prove very satisfactory. Cases must be carefully selected, and the type of torticollis definitely diagnosed, but with these provisos, a full Keen-Stirling operation may be performed, the spinal accessory branch to the sternomastoid on one side being divided, and the posterior primary divisions of the upper three or four cervical roots on the other side. Sometimes the result is extremely good, the resulting paralysis not being too extensive to interfere with the patient's comfort. Medicinal treatment of spasmodic torticollis is notoriously unsatisfactory. Every conceivable variety of sedative or hypnotic has at one time or another been given a trial; none can be relied on.

5. "**Mental Torticollis.**"—Included in this group is habit torticollis, an expression used to indicate attitudes or deformities of torticollic type due to ocular or otic defects, among others, or adopted for other reasons and become involuntary. Mental torticollis is the phrase invented by Brissaud to explain cases where there is a preponderant psychical factor in the disease. It is thus allied to tics of the neck, and its treatment will be best considered under the subject of tics.

S. A. K. W.

DISEASES OF THE SPINAL MEDULLA

Disseminate Sclerosis: Multiple Sclerosis

Little is known as to the origin and causation of this disease, and any treatment directed to the cure of the condition is purely empirical. There is no doubt, however, that treatment on general lines combined with the use of certain drugs does exercise a beneficial effect in retarding the progress of the malady, and further, that a great deal can be done toward the relief of the many symptoms which may be associated with it.

The disease, although tending in most cases to progress, must not be regarded as chronic. Its onset and the exacerbations which are characteristic of the condition are, as a rule, more or less sudden, and the remissions which take place may be remarkable, both as regards their duration and the amount of recovery which takes place.

Prophylactic Treatment.—The onset of the disease occurring as it does in persons otherwise apparently healthy precludes the possibility of effective prophylactic treatment. On the other hand, experience has shown that certain conditions tend to accentuate or rekindle the disease in those in whom it may appear to have become latent: chief amongst these must be placed: (1) Over-fatigue, especially of a physical nature; (2) the state which follows upon any acute febrile disorder; (3) the state subsequent to the puerperium.

It is of the greatest importance, therefore, to insure that any patient who is suffering from disseminated sclerosis or who has previously exhibited signs of the disease should avoid over-fatigue, should have a prolonged period of rest after any acute infective disorder, and in the case of a woman should avoid the possibility of becoming pregnant. Too much stress cannot be laid upon the latter point, as my personal experience has been that in every case where a woman suffering from disseminated sclerosis has subsequently given birth to a child she has had a serious relapse within two or three months of parturition; further in many instances the first manifestations of the disease have arisen during this period.

Treatment of the Acute Stage.—At the onset of the disease or of an exacerbation the patient should be put to bed and ordered complete rest and the general health should be attended to, although as a general rule it will not be found to be affected. The indications for special treatment will be considered under special symptoms, and in a disease with such protean manifestations it is necessary to discover the true cause of any disability complained of. There may be actual loss of power and signs of an affection of the lateral cerebro-spinal tracts, on the other hand there may be little loss of power, but considerable disability owing to ataxia either of cerebellar or more extensive origin, or yet again the disability may arise from subjective sensations of numbness and tingling or sensory disturbances. In chronic cases spasticity may be the most distressing feature, and this is often combined with obstinate sphincter trouble. It must never be forgotten that most cases have superadded to the organic disturbance a greater or less degree of functional paralysis.

Motor System.—Paralysis is rarely complete even in the most severe cases. It should be treated by massage and passive movements to the affected parts, followed by resistance exercises modified to suit each individual case and never such as to cause fatigue. Faradism may be applied to demonstrate to the patient that the nerves and muscles respond normally; this will encourage him, and is specially useful in cases where there is numbness. Ocular paralysis, especially of the abducens nerve, is sometimes present but is rarely permanent, and the patient should be told that the diplopia will disappear.

Ataxia.—If the ataxia is purely cerebellar, in which case it is often associated with vertigo, it will be transient, for even if the lesion be permanent compensation usually takes place. The intention or action tremor which is sometimes so characteristic a feature of the disease arises from a lesion which involves some of the subordinate co-ordinating systems; it may remain permanent, but exercises carried out on the lines laid down by Frænkel (see under Tabes Dorsalis) should be employed and sometimes prove effectual in controlling the ataxia. The exercises should not be started too soon and must not be given so as to fatigue the patient. Where the upper limbs are affected simple exercises can be carried out, by moving pegs of a cribbage-board from one hole to another, or by moving marbles on a solitaire-board; dummy piano keyboards and typewriters may be also employed for the purpose. Where the lower limbs are affected bed exercises can be carried out, but inasmuch

as they involve more strain on the patient, their use must at first be strictly limited. Later on walking exercises can be added to the training.

Spasticity.—For the reflex spasms which may be troublesome after an acute attack, 20 gr. of bromide with 5 min. of tincture of belladonna given at night-time will usually prove effective in controlling the movements. In chronic cases where spasticity is severe great relief will be obtained by treating the lower limbs with hot air and subsequently carrying out passive movements at all the joints. In more obstinate cases the spastic contraction should be counteracted by means of extension pulleys applied to the foot of the bed which is raised; the weight to be applied should be at first 4 to 6 lb. and may later be increased to 10 lb. When first applied the patient may resent their application but they should be persevered with, and it will generally be found that in four or five days' time he appreciates the benefit and realises an improvement in the stiffness. The question of operative interference, to counteract the spasticity by tenotomy, will only arise in very chronic and severe cases, and its advisability must be determined by the study of each individual case. When the immediate effects of an acute attack have passed off the patient should be allowed to walk. On rising the legs feel very stiff, but this tends to diminish after exercise, and the patient is often led to imagine that walking is good for the spasticity. It should therefore be impressed upon him that a small or moderate degree of exercise may do some good, but that over-indulgence will invariably result in increased spasticity.

Sphincter Trouble. *Vesical.*—Incontinence of urine is often a troublesome symptom. It is best treated by the administration of pills containing $\frac{1}{4}$ – $\frac{1}{2}$ gr. of the extracts of ergot and belladonna, given once or twice a day. It is rarely necessary to use a catheter, as retention of urine is very rare. Should cystitis develop it must be treated by irrigation and the administration of 5 gr. of urotropine or helmitol twice daily.

Rectal.—Rectal incontinence is rare; constipation, on the other hand, is one of the most troublesome complications of the disease: its occurrence can be prevented if the patient be properly attended to. The administration of pure petroleum and cascara will prove sufficient, provided the patient has not been allowed to become too constipated, and their action may be made more efficacious by daily abdominal massage. Unless the constipation is properly treated the patient may develop an intestinal toxæmia which may be the direct cause of death.

Optic Atrophy.—Not infrequently a patient with disseminated sclerosis suffers from a sudden loss of vision which may first be almost complete, but is later recovered from, although a scotoma may remain permanently. This is usually due to a patch developing in the retrobulbar portion of the optic nerve: in other cases, after partial recovery, the vision gradually deteriorates and the nerve shows signs of atrophy. If the patch be situated further back a primary atrophy may develop. In every case where visual symptoms occur the use of tobacco should be negatived and the eyes protected from bright light or over-strain.

Medicinal Treatment.—One of the characteristic features of the disease is the tendency to remissions of the symptoms, and this makes it difficult to assign to any drug a definitely beneficial effect, but practical experience shows that the most effective is arsenic, provided it is administered over a considerable period and given in large doses. It is given in Fowler's solution, 3 min. being given thrice daily in a wineglassful of water after meals, 1 min. being added to one dose each day until a maximum of 15 min. is being taken three times each day. Should the patient show signs of intolerance the drug should be discontinued for two or three days and treatment again started with small doses: thus prescribed I have seen excellent results attained in cases which previously resisted other forms of treatment.

Sufficient time has not elapsed to enable one to form any opinion as to the value of salvarsan in this disease. All that can be said is that up to the present its use has not been attended by any definite improvement in the state of the patient. The administration of mercury either by inunction, by the mouth or by injection has not been attended by sufficiently good results as to attribute any special virtue to its action in this disease.

Collargol (a preparation of silver) in 1 gr. pills by the mouth, or $\frac{1}{2}$ to 1 per cent. solution by intravenous injection, has been advocated by Charcot and Erb, and their results might warrant further treatment on these lines.

Phosphorus and preparations containing it have been strongly advocated, but do not appear to have any specific action apart from that of a general tonic.

Fibrolysin.—Injections of fibrolysin have been recommended on the grounds that they might have some effect on the patches of sclerosis, but in my experience this method of treatment has never yielded any good results.

Treatment by X-rays and radium has also been suggested, but at present the results obtained from them have not proved satisfactory.

T. G. S.

SUBACUTE COMBINED DEGENERATION OF THE SPINAL MEDULLA

This disease is characterised clinically by the onset of subjective and objective sensory changes in the distal portions of the limbs followed after a longer or shorter period by signs of an affection of the pyramidal (lateral cerebro-spinal) tracts, segmental anæsthesia and sphincter trouble, terminating rapidly with symptoms of a complete transverse lesion of the spinal cord, flaccid paraplegia, with muscular atrophy, total sensory loss, retention of urine, trophic changes, mental impairment and death. Pathologically the changes met with are diffuse focal lesions, with systemic degenerations in the posterior columns and round the periphery of the spinal medulla. The disease occurs both in men and women, generally beginning between the ages of forty-five to sixty-five. It usually runs a steadily progressive course, but cases which have not gone beyond the first stage sometimes show remarkable remissions under appropriate treatment. The duration of the disease may be as short as one year, the general average, however, is from two to five years, although in a considerable number of cases the duration may be as much as ten years. It is almost invariably associated with anæmia, which may be pernicious in character or merely a severe type of simple anæmia. It was thought at one time that the changes in the spinal medulla were secondary to those in the blood, but it is more probable that they are both dependent upon some unknown toxic cause, although the spinal medulla undoubtedly suffers from the impoverished condition of the blood.

Treatment.—Successful treatment can only be hoped for in the cases recognised in the first stages, all possible sources of anæmia should be sought for and remedied, thus oral or intestinal sepsis, hæmorrhoids or uterine hæmorrhage must be attended to. The patient must be placed in healthy surroundings and instructed to live an open-air life, regular exercise should be enforced, care being taken not to induce fatigue, and with this in view general massage should be given if possible. The diet must be nourishing, and the patient encouraged to take plenty of milk and blood-forming substances. Medicinal treatment will comprise general tonics, more especially iron and arsenic. Arsenic is specially useful, and given in large doses over a considerable period often causes a distinct improvement not only in the anæmia but in the nervous symptoms. I have recently treated two cases with injections of salvarsan, and the immediate effects have been excellent; it is, however, too early to say whether the improvement will be permanent.

Nervous Symptoms.—*Paraesthesia* is often troublesome. It may be relieved by mild faradism or by the administration of bromide and nux vomica.

Reflex Spasms, which are troublesome during the second stage, may be controlled by bromide or pills of ergot and belladonna.

Motor System.—Massage and electrical treatment are useful in the early stages, but are useless in the third stage. Ataxia if present should be treated with Frænkel's exercises.

Sphincters.—In the early stages incontinence and constipation are the chief troubles and must be appropriately treated. In the last stage there is retention of urine which necessitates catheterisation. A distended bladder should never be completely emptied, as this is frequently followed by profuse hæmorrhage. Every precaution must be taken to prevent the occurrence of cystitis.

Trophic Changes.—In the last stage it is practically impossible to prevent the occurrence of bed-sores, and only the most careful nursing on a water bed can hope to delay their advent. T. G. S.

PARAPLEGIA

Paraplegia is a clinical term used to denote a condition of paresis or paralysis of the lower extremities which may be of organic or functional origin. Organic paraplegia may be due to many various pathological conditions and may be spastic or flaccid in type, although in many cases they are combined. Functional or hysterical paraplegia may be present as a symptom of hysteria.

This article is only concerned with the treatment of paraplegia, and no reference will be made to the conditions underlying its production.

Organic Paraplegia

1. **Spastic Paraplegia.**—This type is associated with affections of the lateral cerebro-spinal system which may be of cerebral or spinal origin: it is characterised by paresis or paralysis of voluntary movement and spasticity of the muscles. The muscles retain the normal electrical reactions, and there is no atrophy apart from that which arises from disuse.

Paresis or Paralysis.—The paralysis is primarily due to the lateral cerebro-spinal lesion and is manifested by a loss or diminution of the power of voluntary movement. The disability resulting from the paralysis may be increased by the intervention of other factors: (1) Functional paralysis; (2) adhesions in the joints; (3) spasticity and spastic contractures.

In order to attain the best results the patient

must be continually encouraged. If any voluntary movement be present it should be demonstrated to him and he should be made to practise it. In order to show him that the nerves and muscles are not paralysed, electrical stimulation should be used. Further he should be assisted in making movements by supporting the weight of the limbs, as by this means small degrees of movement may be brought out. Many cases of organic paraplegia are unable to walk, not because of the actual paralysis present but because the patients have become imbued with the idea that they are paralysed and do not make any serious efforts.

Adhesions in the Joints.—Adhesions are apt to develop if the joints are allowed to remain unattended to. This will inevitably lead to limitation of movement. It can be prevented by passive movements of the limbs at all joints, which should be carried out several times daily, and the patient should be instructed to assist the passive movements by voluntary effort. If adhesions have formed they should be broken down by passive movements, if necessary, under an anæsthetic, and their recurrence prevented by subsequent daily treatment. Hot air will relieve the pain and lessen the reaction which follows the breaking down of adhesions. Injections of fibrolysin have been found useful in removing the adhesions.

Spasticity.—Spasticity is due to an increase of tone in the paralysed muscles. It occurs in all the muscles, but becomes more noticeable in the flexor muscles, owing to the occurrence of reflex flexor spasms, which being uncontrolled by voluntary or cortical inhibition tend to overcome their weaker antagonists and permanently upset the muscular balance. This leads to spastic contracture and ultimately to the development of permanent deformity in which the limbs become more or less fixed in certain positions. Thus it is that in typical spastic spinal paraplegia the position which the limbs tend to assume is nearly always the same—flexion and adduction at the hips, flexion at the knee, drawing up of the heel and inversion of the foot. The earliest sign of commencing spasticity is the occurrence of reflex spasms, chiefly at night; if they occur when the patient is walking they cause him to fall. At a later stage it causes a stiffness of the legs, the toes scrape along the ground, and walking is only possible by circumducting the leg. When sitting the legs are apt to go into clonic spasm and when in bed the knees become drawn up and adducted, the feet pointed and inverted with the heels drawn up. If the patient be bedridden the limbs tend to become fixed in these positions; if it be only due to spastic contracture it will be found possible to move the limbs freely under anæsthesia. On the other hand, if there be organic contraction of the muscles, tendons or ligaments free movement will be found impossible.

Treatment.—(*a*) Excessive exercise must be forbidden, as it invariably increases the spasticity. It is sometimes difficult to make the patient realise this, as finding that a little exercise after he gets up reduces the stiffness of his limbs, he often concludes that the more exercise he takes the better he will be.

(*b*) Passive movements are undoubtedly the best means of combating early spasticity and of reducing the stiffness in the muscles; they should be carried out three or four times daily and should never be discontinued as long as spasticity remains. The reflex spasm at night may be set up by the weight of the bedclothes, but this can be remedied by placing a cradle over the limbs.

(*c*) Heat has an excellent effect in reducing spasticity. A warm water or hot-air bath taken immediately before beginning the passive exercises facilitates their execution and increases their effect.

(*d*) *Mechanical Restraint.*—The reflex spasms which occur at night may be controlled by fixing a draw-sheet firmly across the bed so as to pass over the patient's legs above the knees. In other causes extension can be applied by means of weights and pulleys fixed on the foot of the bed. The weights can be gradually increased, and this method of treatment, if applied early and persevered with, will be found most effective.

In more severe degrees of spasticity the contracture can only be overcome by prolonged over-extension of the contracted muscles. This can be carried out by placing the patient in a metal frame constructed on the principle of a double Thomas's splint and so arranged as to secure extension and abduction at the hip, extension at the knee and fixation of the ankle and foot at right angles. In slight cases the desired effect may be obtained by the patient sleeping in the instrument. It may be found necessary, however, in order to get the limbs into the correct position to have recourse to various surgical measures.

Surgical Measures.—Spasticity has been attacked surgically by two distinct methods—

(*a*) Tenotomy and division of contracted structures, muscles, fasciæ, etc.

(*b*) By division of posterior roots which produces a loss of tone in the muscles and diminishes the spasticity. This method was brought into practise by Fœrster.

(*a*) **Tenotomy and Division of Contracted Structures.**—The principles which underlie this method are division of the muscles or tendons which are contracted and over-acting. This abolishes the spasticity in these muscles and

causes a cessation of reflex spasms. It permits the fixation of the limb in the desired position and restores the muscular balance. The requirements of each case must be dealt with individually, and care must be taken to make certain that the full amount of movement required has been obtained by the operation. In respect of the hip, extension must be obtained without the occurrence of lordosis and any inward rotation of the hip must be remedied. In dealing with the ankle a lengthening of the tendo calcaneus by incision and suture is preferable to complete division, the amount required being estimated by dorsi-flexing the patient's ankle while his leg is extended at the knee. These operations may be performed in several stages. If the division of the contracted muscles has been sufficiently performed the patient will feel no pain subsequent to the operation.

In order to secure permanent benefit from operative treatment the limbs must be kept fixed in the proper position by splints or other means. When the wounds have healed the splints are removed daily and passive movements carried out and the patient encouraged to perform voluntary movement at all the joints. The effect of such treatment will be that the patient's limbs are freely movable at all joints and that he has power of voluntary movement to a greater or less degree according to the paralysis. The treatment of the later stages depends upon the individual case, but all voluntary movements must be carried out correctly, and to insure this various exercises should be given—local for each joint and general for the whole limb and for both limbs—crawling, kneeling, sitting down on the heels, walking, etc., etc. Before walking is permitted the patient must learn to stand correctly, and for this reason crutches should not be given; if necessary long splints or a go-cart should be used.

(*b*) **Division of Posterior Roots.**—Förster introduced the division of the posterior spinal roots as a means of counteracting spasticity and spastic contractures. This method has been attended with considerable success, but the operation requires much experience in order to determine which roots are which, and at the best the results are no better, if as satisfactory, as those obtained by surgical interference with the muscles themselves, provided the necessary subsequent treatment is carried out.

Genito-urinary and Rectal Symptoms.—*The Bladder.*—Retention of urine may follow the sudden onset of paraplegia or where the lesion of the spinal medulla is complete; it rarely persists for long. In all cases the condition of the bladder should be investigated, and if retention be present a catheter must be used twice or thrice a day; the greatest care must be taken to prevent infection.

Incontinence of Urine.—In one form of incontinence the bladder is never completely emptied, although the patient may pass water reflexly very frequently. In these cases a catheter should be passed immediately after the patient has urinated in order to ascertain the amount of residual urine. If there be residual urine the bladder should be irrigated at least once a day. In all cases where the urine is decomposed or septic, irrigation should be carried out twice a day. The condition of the urine will be improved by the administration of urotropine, helmitol, or ammonium benzoate. Patients with incontinence should be encouraged to make voluntary attempts to pass their water at intervals of two hours, and should have it drawn off last thing at night. Pills composed of $\frac{1}{4}$ or $\frac{1}{2}$ gr. of the extracts of ergot and belladonna are sometimes useful in checking incontinence. In another form where there is complete loss of sensation in the sacral areas the urine may dribble away continuously; this cannot be remedied by any drug or routine methods.

The patient must not be allowed to lie in soiled bed-linen, and this will require constant attention. Various mechanical contrivances have been devised to overcome this difficulty but few are satisfactory. A sponge bag arranged with tapes and containing some absorbent cotton-wool is probably the most efficacious.

Rectum.—Incontinence of fæces may occur in acute lesions or in lesions affecting the lumbo-sacral trunk or roots. It may be controlled to a certain extent by plugging the rectum, but continuous care is essential. As a rule constipation is more common and is best treated by paraffin, cascara sagrada, abdominal massage, and enemata. Purgatives should only be given at times which will permit of the patient being attended to at the time of their action.

Priapism occasionally occurs when the lesion is situated in the upper dorsal region. Bromide or monobromate of camphor are sometimes helpful in controlling this distressing symptom.

Bed-sores can only be prevented by most careful attention to the cleanliness of the patient and to the condition of the bed. In all acute cases a water bed should be used. Pressure should be relieved as far as possible by changing the patient's position and by protecting points of pressure by means of air cushions or pads. The skin should be well washed, thoroughly dried and rubbed with methylated spirit once or twice a day. In cases with incontinence the surrounding parts can be protected to a certain extent by the use of ointment. If bed-sores have formed chlorinate of soda or peroxide of hydrogen are

most serviceable in clearing up the sore. In chronic cases red lotion can be used occasionally as a stimulant. A word of warning is necessary in regard to subcutaneous or deep-seated abscesses which occasionally arise in the gluteal region and may remain undetected unless sought for, they can usually be palpated, and if present should be opened and washed out with a weak solution of chlorinate of soda.

2. **Flaccid Paraplegia** usually arises from lesions of the lower motor neurone; it may occur in cases of peripheral neuritis from local lesions affecting the nerve roots in diseases affecting the anterior column cells in the lower dorsal, lumbar, and sacral parts of the spinal cord, whether of toxic infective or infective origin.

Treatment.—In cases of peripheral neuritis and in complete transverse lesions of the spinal medulla, pain may be a great hindrance to treatment in the early stages, and should be overcome as far as possible by rest, local applications or the administration of appropriate drugs. When the acute stage has passed off treatment of the paralytic condition should be started. The following are the general principles: (1) Prevent overstretching of the muscles by removing the weight of the bedclothes from the feet, and if necessary supporting the limbs in the correct position by means of splints or other apparatus. (2) Passive movements should be given daily, as they prevent the occurrence of adhesions in the joints, stimulate the muscles and counteract the tendency to contracture and deformity from the over-action of stronger or less paralysed muscles. (3) Massage is specially useful in such cases in stimulating the muscles, promoting the circulation and improving the trophic condition. In neuritic cases it may be necessary to employ very gentle massage in the earlier stages. (4) Electricity. Electrical treatment is most serviceable and may be given in a bath or by applying a large electrode under the back, the muscles being stimulated by a roller electrode or by local application of a button electrode. If the muscles respond to faradism this may be employed. Where faradism fails to produce response or where the necessary current is too painful to be borne, galvanism should be used, as it is specially helpful in stimulating paralysed muscles and improving their condition. (5) Voluntary movement must be encouraged, the patient's efforts being assisted by passive movements or electrical stimulation or by lessening the weight of the limbs in placing him in a warm bath and encouraging him to move his limbs about. Later, or where paralysis is less severe, special exercises and movements against resistance should be performed, and finally walking exercises, care being taken to insure that the patient, when possible, uses the correct muscles in a proper fashion. Many children who have suffered from anterior poliomyelitis are allowed to develop spinal deformities and bad methods of walking simply because they are not compelled to use the proper muscles but are permitted to make use of other muscles by placing the limbs in an abnormal position. A common example of this is seen in cases where a child neglects to use the flexors of the hip, although they are not seriously paralysed, and advances by rotating the hip outwards and using the adductors to bring the limb forwards. It is often advisable in such cases to devise some temporary apparatus which will insure the use of the correct muscles. (6) In cases with contractures applications of hot air may be helpful in reducing the contractures and in facilitating passive movements. (7) If the lesion be stationary and the paralysis becomes chronic, walking instruments or appropriate surgical operations may be necessary, such as tenotomy, muscle transplantation, nerve grafting or nerve transplantation.

Flaccid Paraplegia may be combined with spastic paraplegia or may result from the extension of a lesion of the spinal medulla, which has caused spastic paralysis. In the latter the paraplegia is associated with sensory loss, trophic disturbances and sphincter impairment, and unless the primary cause of the condition can be removed little can be done in the way of treating the paralysis. Care must be concentrated upon the prevention of bed-sores and the relief of the sphincter troubles.

Hysterical Paraplegia.—The cure of this condition will depend on the cure of the hysteria underlying its production. The paralysis should be treated by keeping the patient in bed until he is able to move the limbs freely and with good power, and later by seeing that he is only allowed to walk in a normal manner. This can only be secured by personal attention and supervision. Massage, electricity—often with strong currents—and exercises will all prove helpful, but the patient requires to be given encouragement and to be treated with kindly firmness.

T. G. S.

EXTRA-MEDULLARY SPINAL TUMOURS

Compression paraplegia may arise as the result of extra-medullary tumours which originate in the vertebral column or are situated within the vertebral canal. The symptoms found in cases of vertebral tumour are referred to the spine, the nerve roots and the spinal medulla according to the seat and extent of the growth. For convenience in description spinal tumours may be classified into intra-dural and extra-dural.

Intra-dural Tumours.—These tumours may arise from the leptomeninges, from the nerve roots or from the dura mater. They fall into two classes, the one in which the tumours are slow-growing and more or less benignant in character and those which are of rapid growth and malignant in type tending to extend and involve the spinal medulla.

Slow-growing Intra-dural Tumours. — These may originate from the leptomeninges or from the sheaths of the nerve roots. They are usually fibro-sarcomas, neuro-fibromas or fibro-myxo-sarcomas. They arise commonly on the lateral aspect of the spinal medulla, are ovoid in shape and tend to extend upwards and downwards parallel to the spinal medulla. The symptomatology, therefore, is often strikingly similar and consists, in the cases where the growth is attached to the roots, first of root symptoms, sensory and motor, referred to one or more roots on the side of the spinal tumour, followed by the gradual onset of signs of unilateral compression of the spinal medulla, or, in cases where the roots are not involved, of the gradual onset of unilateral medullary symptoms. The root symptoms are on the side of the tumour and when present must be taken as indicating the level of the lesion. The medullary symptoms which will be found on the *side of the tumour* are spastic paralysis, with loss of the corresponding epigastric and abdominal reflexes below the level of the tumour, increase of the deep reflexes and extensor plantar response. On the *side opposite* the tumour sensory symptoms may be found, a loss or diminution of sensibility to pain, heat, cold and touch. The upper level of this sensory loss will not correspond directly to that of the tumour, and a level four segments above should be taken as the level of the tumour. The reason of this is that sensations of heat, cold, pain and touch are not conveyed up the spinal medulla on the same side as they enter, they cross to the opposite side of the spinal medulla—pain, heat and cold more rapidly than touch—but this crossing is gradual and is not completed until five segments above their point of entrance. If the spinal medulla be compressed at the level of the first dorsal segment on the left side, the sensory loss will only extend up to the level of the fifth or sixth dorsal segment on the right side, as the sensory paths which convey sensations from the fifth, fourth, third and second dorsal roots on the right side have not yet reached their position in the left lateral tract, and therefore do not suffer from the unilateral compression. Failure to recognise this fact has led to faulty localisation of the level of the tumour.

If the tumour continues to grow, bilateral medullary symptoms will develop—spastic paraplegia with sphincter trouble and sensory loss on both sides *up to the level of the lesion.* The sensory paths in this case being interfered with on both sides of the spinal medulla, the upper level of the sensory changes may be taken as indicating that of the tumour.

Slow-growing intra-dural tumours may also arise from the dura and may give symptoms very similar to those growing from the leptomeninges or nerve roots, but as a rule the unilateral character of the symptoms is neither of so long duration nor of so striking a character. The nature of these tumours may be fibro-sarcoma, psammoma or endothelioma, the latter being the most common.

Rapidly growing Intra-dural Tumours are either soft round-celled sarcomas or growths arising secondarily to tumours elsewhere. They may be metastatic or spread in along the nerve roots—examples of this are secondary tumours from tumours of the choroid plexers and from mediastinal growths. As a rule they occur in young people and extend rapidly, surrounding and involving the spinal medulla, causing a complete paraplegia within six months. A rare form of tumour which may develop at any age is angioma, which may extend round the spinal medulla.

Extra-dural Tumours.—These may originate in the extra-dural space or in the vertebral column. They may develop in connection with the dura mater—endothelioma and fibro-sarcoma; or from the periosteum—sarcoma; or they may be secondary to growths elsewhere generally from direct extension, especially in cases of mediastinal growth. Lipomata growing in the perithecal space may occasionally cause compression of the spinal medulla. Hydatid cysts may be found in this situation, causing symptoms of compression paraplegia, but such cases are rare in Great Britain. In general, extra-dural tumours have as initial symptoms local pain and sometimes tenderness on pressure over the spine. Root symptoms are common and often early, and the medullary symptoms may develop late or early, but they are usually bilateral from the onset, there seldom being any lengthy period with unilateral medullary symptoms. Tumours affecting the vertebral column are carcinoma or sarcoma. Carcinoma is always secondary and may follow cancer of the breast, alimentary tract, kidneys, lungs, etc. Sarcoma is sometimes primary but often secondary. As a rule cases of malignant disease of the spine have definite bone symptoms in pain on pressure, deformity and restriction of movement. Root pains, especially on movement, may be an early symptom, but the medullary symptoms are generally late in appearing although they progress rapidly.

Treatment.—Any case developing symptoms

of compression paraplegia with gradual onset should be regarded as being possibly one of spinal tumour. The differential diagnosis between general disease of the nervous system with paraplegic symptoms, chronic intra-medullary lesions, syphilitic meningitis and spinal caries may present some difficulty, but careful examination from the clinical and clinical-pathological side should suffice to distinguish most cases. Further, an X-ray examination should be made in all cases, as although it may often not throw much light upon the diagnosis it will reveal the presence of aneurysm—a condition, the possibility of which must always be borne in mind and may be of great value in cases of spinal caries or malignant disease of the spine.

Having decided that the case is one of spinal tumour, the next question is to determine the level of the lesion. This will not present much difficulty if what has been said above in regard to cases with unilateral medullary symptoms has been appreciated.

In cases of slow-growing intra- and extra-dural tumours operation for the removal of the tumours should be undertaken as soon as the diagnosis is made, as the longer the delay the larger will the growth become and the greater the risk of permanent damage to the nerve roots and the spinal medulla.

Cases of malignant disease of the vertebral column should not be operated upon except as a palliative measure for the relief of root pain, when the roots involved should be divided intra-durally. Cases continually crop up which, while presenting many of the features of spinal tumour, yet do not permit of an exact diagnosis as to the intra- or extra-medullary situation of the lesion or as to the nature of the compression. In these cases exploratory operation should be advised. In competent hands the patient is not exposed to undue risk and the operation will not aggravate his condition, and even if a tumour be not found the operation may reveal some local condition, such as chronic meningitis or arachnoid cyst, which experience has shown to be often amenable to operative interference. The treatment of the paralysis, sphincter troubles and trophic changes which may be incidental to spinal tumours is given under the treatment of paraplegia.

SYRINGOMYELIA AND INTRA-MEDULLARY SPINAL TUMOURS

This disease is characterised pathologically by the formation of cavities within the spinal medulla. These cavities may be due to a primary gliosis with secondary rarefaction, or to degeneration of gliomatous tumour formation which has developed within the medullary substance. In whichever manner the disease arises the clinical picture is similar, as the symptoms depend more upon the situation than upon the nature of the lesion.

Prophylaxis.—Some authorities consider that there is sufficient evidence to warrant the assumption that in certain cases the condition may arise as a result of injury, but however that may be it may undoubtedly be aggravated by injury; patients must, therefore, be warned against exposing themselves to the risk of injury, especially jars of, or blows upon, the spine.

Treatment of Conditions arising as a result of the Disease. *Local Trophic Disturbances.*—Whitlows, perforating ulcers, and arthropathies are liable to occur spontaneously and are readily induced by any local injury. This danger is increased by the insensitiveness of the parts to painful and thermal stimuli, and it is essential to impress upon the patient the necessity for guarding against every kind of injury and of securing immediate medical attention should any sores develop. The treatment of trophic sores must be carried out with aseptic precautions.

Arthropathies may be alleviated by the judicious application of supports or apparatus, but active surgical interference is to be deprecated.

Motor Symptoms.—Atrophic motor palsies should be treated by massage and faradism.

Spastic paralysis must be treated by passive movements, massage, etc. Reflex spasm if troublesome may be controlled by moderate doses of bromide, or by the administration of pills of ergot and belladonna, $\frac{1}{4}$ gr. of the extracts once or twice a day.

Treatment of the Disease.—So far little has been achieved in this direction, but in all cases where the condition is progressive prolonged rest should be enforced and will often be found to be attended by a rapid and permanent improvement in the extent and severity of the symptoms.

Röntgen Rays.—Treatment by means of Röntgen rays applied to the spine and the affected levels has in some cases proved beneficial and deserves further trial. Rays of moderate strength should be applied once or twice a week.

Radium.—The local application of radium to the affected segments has been reported on favourably, but as yet our experience does not warrant its general application.

Surgical Treatment.—During the past few years laminectomy has been practised in a considerable number of cases; in some of these good results have been obtained where the opening of the membranes has resulted in a local spinal decompression. In one or two instances the cavities have been opened by

incision through the posterior median fissure and pressure symptoms relieved. Any further attempt to extirpate the growth is to be deprecated.

Although we cannot hope for much success in the actual treatment of the disease, yet the possibilities of decompression and the local application of Röntgen Rays or radium deserve greater attention than they have yet received.

Hæmatomyelia.—Hæmorrhage into the spinal medulla may take place almost spontaneously into a syringomyelic cavity or as the result of some slight strain, as in coughing, retching or lifting some object from the ground. It may also occur from more severe injuries—jars on the spine or severe spinal injuries. In some cases there may have been evidence of syringomyelia antecedent to the hæmorrhage, in which case there is a sudden increase in the symptoms often with pain referred to the root areas of the segments affected and with an increase or beginning of intra-medullary symptoms—motor, sensory and reflex. In cases where the hæmorrhage is spontaneous the symptoms are of sudden onset and rapidly extend to the extent of the cavity and then cease. A sudden onset of intramedullary symptoms extending over two or three segments is therefore more or less typical of hæmorrhage into a pre-existing cavity.

Treatment.—Absolute rest in bed on a water bed with special precautions against trophic changes. The patient must be forbidden to move or exert himself. The bowels should be freely opened and morphia should be given if there be much pain or restlessness. The bladder must be attended to, retention being an early and transient symptom. Urotropin 7 gr. should be given three times daily. The rest of the immediate and subsequent treatment is similar to that of acute myelitis or syringomyelia, massage, passive movements and exercises being given as necessary. Faradism and galvanism may be applied to the wasted muscles if atrophy should occur. Ice to the spine has been recommended, but its action is very doubtful and it often causes great discomfort to the patient. Doses of iodide of potassium 10 gr. and Liq. Arsenicalis 3 min. should be given from the second day onwards for six weeks. If severe injury has been done to the spine operation should be performed when the acute symptoms subside, but if the symptoms tend to increase after six hours immediate operation should be performed. A lumbar puncture will help to decide the question as to whether there has been hæmorrhage into the meninges, as in such cases blood will be found in the cerebro-spinal fluid. Clinically cases of meningeal hæmorrhage are characterised by great pain and rigidity of the muscles.

T. G. S.

PROGRESSIVE MUSCULAR ATROPHIES

Amyotrophic Lateral Sclerosis.—vide *Progressive Muscular Atrophy.*

Progressive Muscular Atrophy.—This disease and amytrophic lateral sclerosis are essentially the same, and their treatment may be considered together. In all recent cases that come under observation the Wassermann test should be applied, as in some instances the condition is a syphilitic or parasyphilitic case. Should the test prove positive, antispecific remedies should be tried in the shape of salvarsan or neosalvarsan, repeated under the control of the Wassermann test, followed by inunctions of mercury and the exhibition of iodides. Apart from these cases, which are rare, the disease, being due to progressive degeneration of neurons, is not susceptible of cure, but improvement may be obtained, or the advance of the muscular wasting arrested for a time, at all events.

Tonics, such as arsenic, syrup of phosphate or iodide of iron, and strychnine or nux vomica, are useful in maintaining the general health. Cod-liver oil and malt may also prove of service in this connection. These, with good food, rest and protection from pulmonary diseases, form the basis of all treatment in these cases.

Massage and passive movements in the more spastic cases, combined with the faradic or galvanic electric currents, are often useful. The muscular atrophy and weakness seem to be held in check for a time by the hypodermic injection of strychnine, of which $\frac{1}{100}$ gr., increasing to $\frac{1}{40}$, may be administered daily. Where the muscles supplied by the nuclei in the medulla oblongata (Bulbar Palsy) are involved, great difficulty may be experienced in feeding the patient when the disease is at all advanced.

As a rule such patients swallow semi-solid food better than either solids or liquids.

As the disease advances still further, feeding by tube may be necessary. Great care must be exercised, or the patient may either choke or develop a septic bronchopneumonia.

In cases in which the bulbar symptoms predominate the same general rules of treatment are applicable as those described in this section for progressive muscular atrophy.

Werdnig-Hoffmann Type of Progressive Muscular Atrophy of Infants.—This disease is allied to progressive muscular atrophy in adults. Treatment can only be directed towards maintaining the general health, and preventing the occurrence of pulmonary disorders, which are peculiarly liable to prove fatal, owing to the paralysis of muscles of the thoracic wall and the diaphragm. Massage and passive movements may prove useful.

Caisson Disease.—The symptoms of this

disease are caused by bubbles of nitrogen gas liberated in the blood and tissues when decompression has taken place too quickly in the case of divers, or men working under increased atmospheric pressure in caissons.

The only effective method of treating the symptoms, which consist of severe pains in the milder cases ("Bends"), and unconsciousness, cyanosis and paralysis in the severe ones, is to recompress the individual. To be of any use this treatment must be applied at once, and the pressure maintained for several hours, with very gradual decompression.

Prevention in these cases is most certainly better than cure, and this can be done by following very closely the rules laid down for men working under these conditions.

Mild cases of "Bends" may be treated by massage and fomentation. If paralysis has supervened it must be treated on general principles. C. M. H. H.

MENINGOCELE

The treatment of meningocele, whether cranial or spinal, rests with the surgeon. If operative interference is decided on, the base of the sac is isolated as far as possible and it is either ligatured or cut round. Care should be taken to avoid any sudden loss of cerebrospinal fluid. The base must be securely ligatured, and where practicable deep stitches should draw the overlying muscles (in spinal cases) together so as to render the result more secure. In cranial cases, if the skull opening be small, the whole tumour may be excised. Treatment short of operation, viz., tapping the tumour with subsequent injection of Morton's fluid, has sometimes proved satisfactory. Unless the sac is gradually increasing in size, and its membranes gradually thinning, it is often sufficient to protect it adequately, and let it alone.

S. A. K. W.

DISEASES OF THE PERIPHERAL NERVES

Palsies of Cerebral Nerves.—With the exception of the facial nerve, isolated paralysis of the cerebral nerves rarely occurs, except as a complication of some other disease. Treatment of these cases, therefore, resolves itself, as a rule, into the treatment of the underlying major affection. Direct treatment of the affected nerve, or the muscles supplied by it, again with the exception of the facial, is rarely possible.

It will be convenient to consider the cerebral nerves *seriatim*, indicating the possibilities of treatment in each case.

Olfactory Nerve.—Disturbance of smell, due to injury or disease of the nerve, occurs secondarily to disease of the nasal mucous membrane, the state of which requires investigation in every case, and, if diseased, appropriate treatment.

Fracture of the base may cause anosmia, as may tumours situated in the frontal area of the brain. These will give rise to additional symptoms, the anosmia *per se* requiring no treatment. Further, anosmia, usually unilateral, occurs not infrequently as an hysterical symptom, and is then always accompanied by other hysterical stigmata, and requires no local treatment.

Lastly, anosmia is met with as the result of exhausting diseases, particularly as a post-influenzal symptom. In such cases the sense of smell returns, as a rule, with the return of health, its recovery possibly being accelerated by the exhibition of tonics such as quinine and strychnine.

Optic Nerve.—Disturbance of visual activity and limitation of the visual fields occur as a symptom in a variety of conditions, the treatment for which will be found under that of the primary affection.

Oculo-motor Nerves.—These nerves are frequently at fault, either secondarily to errors of refraction, or in the course of organic or functional disorders of the nervous system.

In a case of strabismus, careful examination must be made for errors of refraction, and if found these must be treated by appropriate glasses. In certain cases of this kind tenotomy of the tendons of the medial or lateral recti may be necessary. For detailed treatment of strabismus the larger works on the subject should be consulted.

As a sign of organic disease of the nervous system oculo-motor paralysis occurs most frequently as the result of syphilis, the paralysis being usually due to a syphilitic meningitis. It occurs, however, in other organic diseases of the nervous system, notably in tabes dorsalis (where its method of causation is probably as above), disseminated sclerosis, and in intracranial tumours. Partial ocular palsies, especially ptosis, is also met with in hysteria, but sometimes hysterical strabismus is associated with this.

Paralysis of the intrinsic muscles of the iris occurs through involvement of the sympathetic in aneurysm, enlarged cervical glands, diseases of the pleura, etc. When the diagnosis has been made treatment must be directed to the primary affection.

Syphilitic palsy is best treated by the injection intravenously of salvarsan or neosalvarsan, followed by mercurial inunction and the administration of potassium iodide. When considering the question of injecting salvarsan the contra-indications to its use must be remembered (vide *Syphilis*).

Triginimal Nerve.—Paralysis of this nerve is rare as an isolated phenomenon. It usually occurs as a complication of tumour, tabes dorsalis, or syphilitic meningitis, and rarely from trauma. Trophic changes in the cornea, after injury to or removal of the semilunar ganglion, may call for treatment as for corneal ulcer.

Facial Nerve.—This nerve is more frequently affected than any other of the cerebral nerves. The cause of the paralysis must be carefully ascertained, as the nerve may be affected either within the pons, or on its surface, in the petrous bone, or outside of the skull. Intracranially the nerve is usually affected as the result of middle-ear disease, for which appropriate treatment must be undertaken. When the attack of facial paralysis is apparently due to cold or exposure ("rheumatic" type), a blister should be applied at once behind the ear on the affected side, but this is only likely to be of use when the case is seen quite early.

For the relief of pain, which is sometimes severe, hot applications are useful, and the administration of aspirin, salicylate or phenazone.

Beyond this the treatment to be adopted is massage and the application of electricity to the affected area. This should be begun as early as possible.

The type of electrical current to be used will depend on the electrical reactions of the muscles. So long as the muscles respond to the faradic current, this should be employed.

If the response to faradism continues for a week or more the probability of a speedy recovery is very strong. When the muscles will not respond to faradism, the galvanic current must be used of sufficient strength to produce a moderate muscular contraction. If all response is lost, the application of electricity should be continued, as it seems to maintain the nutrition of the muscles.

In severe cases, much improvement should not be looked for before the end of the third month, but if at the end of six months there is no improvement, it is improbable that any will occur.

In a severe case which recovers partial voluntary power, there is almost always *secondary contracture* of the affected muscles, which may progress to a very considerable extent; should this appear it is probably best to discontinue the use of electricity, but to persist diligently with massage and vibration over the affected side.

On the other hand, when no recovery takes place, the healthy muscles contract, and the paralysed side of the face becomes quite flaccid, with marked sagging of the lower lid. In these circumstances the question of nerve anastomosis by operation should be considered.

The operations which may be done consist in division of the facial nerve close to its exit from the skull, and the implantation into the divided peripheral end of the nerve either of the hypoglossal, or part of the accessory. The former is probably preferable, as the hemi-atrophy of the tongue which results gives rise to no local inconvenience, while in the case of the accessory it is usual to find associated movements of the neck and shoulder accompanying any facial movements which may occur.

The results of this operation are chiefly of advantage from the cosmetic point of view, and where there is no facial deformity should not be undertaken.

The Acoustic Nerve.—(a) Disease of the cochlear division of this nerve may produce tinnitus as the result of irritation or deafness from paralysis. Nerve deafness, unless it is due to syphilis, is not at all amenable to treatment. In the latter case active antispecific treatment may improve the hearing.

With regard to tinnitus, it may be said at once that its treatment is most unsatisfactory. In every case the ear should be most carefully examined for a local cause, such as cerumen, scarring of the membrana tympani, presence of cholesteatoma, etc. When no such local cause can be discovered treatment may be directed against the anæmia, arterio-sclerosis, high blood pressure, gout or whatever may be suspected as the exciting cause.

For the relief of the symptom itself the bromides are of the greatest use, but they will frequently fail to cure the condition.

(b) *Vestibular Portion of the Acoustic Nerve.*—Aural vertigo or Ménières Disease, is the condition for which treatment is usually required in connection with the vestibular nerve. In the acute cases the patient must remain in bed, and be placed under the influence of bromides as speedily as possible. The patient must be kept perfectly quiet, and not allowed to move the head for any purpose. Counter-irritation, by applying blisters to the mastoid process, has been recommended. In the intermittent or chronic forms of the disease the patient should be kept on a small dose of bromide, 10 gr., twice daily between the attacks. It is, of course, of the utmost importance to exclude the presence of a new growth, or epilepsy, as the cause of the condition.

Cerebral Nerves: Glossopharyngeal, Vagus, Accessory and Hypoglossal.—There is little to be said with regard to the treatment of disease of the above.

They are usually affected as the result of new growths invading the floor of the skull, or of syphilis. In the former case there is nothing to be done, whilst in the latter the usual antispecific treatment must be energetically carried

out. It is important to remember the liability of the vagus nerve to neuritic changes in the diphtheritic or alcoholic forms of the disease (*q. v.*).

NEURITIS

There are certain general principles which must be remembered in treating cases of neuritis.

1. **Motor Paralysis.**—(*a*) It is most important to prevent contractions occurring as the result of shortening of the more healthy muscles. This can be obviated by careful passive movements and massage of the healthy as well as the diseased muscles.

(*b*) It is most important to prevent stretching of the paralysed muscles and their tendons. Such stretching may occur either from gravity or from contraction of the active antagonist muscles. Where foot-drop is present, the weight of the bedclothes must never be allowed to rest on the dorsal aspect of the feet. The foot should be maintained in the rectangular position by means of soft leather boots, extending well up above the knee, with rubber band passing from the toe to the ankle, as suggested by Gowers, or any other similar device. In the early stages if there is much pain the same result may be obtained by sand-bags.

In the wrist-drop of lead palsy, the extensor tendons should be prevented from stretching by keeping the wrist over-extended, by means of gloves, fitted on the back with elastic straps passing to a wrist-band.

(*c*) The nutrition of the affected muscles should be kept in as good a state as possible, by starting gentle massage and passive movements very early, in fact as soon as the muscles can be handled without severe pain. Electrical treatment is also very helpful in this respect, but should be utilised later than the massage and passive movements.

2. **Electrical Treatment.**—This can be utilised from two points of view—

(*a*) *For the relief of pain*, and to a certain extent as a curative agent, as, for instance, in the rheumatic form of neuritis.

The desired result may be obtained by the method of cataphoresis, by means of which a drug, or rather one of its component ions, may be introduced locally. The method consists in applying a thick pad of lint, of considerable size, soaked in the drug decided upon, over the painful area or affected nerve, and applying a similar pad soaked in normal saline over some indifferent area. If, for example, it is desirable to ionise the sciatic nerve of one leg, the pad with normal saline should be applied to the other, or over the spine.

Before the constant current which is used in this procedure is turned on, it is well to treat the limb by hot air, or failing this by the application of hot fomentations for half an hour or so, in order to get the skin thoroughly moist and its resistance thereby reduced.

The most useful drugs in this connection are the salicylate of soda (2 per cent. solution) and iodine applied as the tincture. The salicylates are applied under the negative pole, but if iodine is used it should be placed under the positive pole. The current is then gradually turned on. With the salicylates, if the skin is thoroughly moist and large pads are used, a current of 50 ma. produces no pain at all, and is better than a smaller current. With iodine, on the other hand, it is impossible to use so large a current, and not more than 5 to 10 ma. should be given. Care is necessary in following out these instructions, otherwise burns may result.

The current should never be stopped abruptly, but should be gradually turned off. The duration of the applications should be from fifteen to thirty minutes.

This method practically never fails to relieve pain, but it must be continued for a considerable number of applications. These are usually given on alternate days. In addition to ionisation, high frequency and X-rays are useful.

(*b*) *For the Improvement of the Muscular Condition.*—For this object, either the galvanic or faradic currents may be employed, the choice being determined by the muscular reactions. In most cases of motor palsy, due to neuritis, the muscles no longer respond to faradism, in which case the constant current should be employed. The strength of current to be used should be that which will produce a moderate response from the affected muscles without giving pain. As a rule from 5 to 10 ma. will suffice. The active electrode should be used in the labile manner, *i. e.* stroking up and down the affected limb. A recent method of electrical treatment, suitable when there is *extensive* muscular involvement, is that introduced by Bergonié, which, however, requires a special installation. It has proved most effective in one or two cases of which I have had personal experience, and the results of its application are stated to be most encouraging by those who have used it much. (See article on *Electro-therapeutics*.)

We can now consider the treatment of the various varieties of neuritis.

1. **Multiple Neuritis.**—The cause of this condition is practically always some chemical poison, which, however, may arise from a number of different sources. Thus there are the microbic cases, of which diphtheria is the classical example; but included in this group we also find influenza, enteric, leprosy and septicæmia; the metallic poisons, such as lead, arsenic and mercury; chemical poisons,

such as alcohol, carbon bisulphide and naphtha; metabolic diseases, such as diabetes, gout, rheumatism; parasitic conditions, as malaria and syphilis, and so on. In the treatment of any particular case it is of the utmost importance to determine, if possible, the primary causal factor, and treatment will then be directed to it. In a certain number of cases it will be impossible to arrive at the causal factor and the case must then be treated on general lines. In all acute cases the patient must be confined to bed, and kept completely *at rest.* This is particularly important where there is any evidence of cardiac involvement, especially in post-diphtheritic neuritis, in which case the patient should be allowed to make no effort, or exert himself in any way whatever. The severe cases should be placed on a water-bed, and the skin carefully attended to, to prevent the formation of bed-sores. The bedclothes should be prevented from pressing on the limbs by a cradle, and the limbs should be maintained in proper positions by means of sandbags in the early stages, or mechanical devices when the acute stage has passed.

The bowels should be kept freely open, and the action of the skin and kidneys encouraged, by diaphoretic and diuretic drugs, as, for example, the citrates, liq. ammonii acetatis, caffeine or its citrate, and salicylates.

The diet should be light and easily digested, and in special cases, as for example in alcoholic neuritis, where there is almost always gastritis, the dietary may have to be confined to liquids and jellies. Alcohol, as a rule, is not indicated, but under special circumstances it may be necessary to give it in small divided doses, should the pulse flag. There are no drugs which can be regarded as specifics, except quinine in the case of malarial neuritis, and mercury with potassium iodine or salvarsan in cases of syphilitic origin.

It has been the fashion to treat cases of lead neuritis by the simultaneous administration of the iodides and magnesium sulphate on the assumption that the former assisted elimination of lead by forming a soluble compound, while the latter formed an insoluble one. There is, however, no scientific support for this theory (Dixon Mann).

Magnesium sulphate is, no doubt, useful as an aperient in these cases, as constipation is a very constant symptom.

For the relief of pain in the acute stage, warm fomentations, followed by the application of gamgee or "thermogene" wool covered by a light bandage, are often effective, so also in certain cases is the application of equal parts of mesotan (methyl salicylate) and olive oil, which should not be rubbed in, but lightly painted over the painful area. Very rarely morphia may be required. Analgesic drugs such as aspirin, antipyrin and phenacetin must be used as required.

The tinct. gelsemii in 10 min. doses is sometimes effective.

Sleeplessness is sometimes a marked feature, and should be treated on general lines. When caused by severe pains, the administration of phenazone, aspirin or a mixture of phenacetin, aspirin and caffeine citrate, 5 gr. of each, will often relieve the pain, and by so doing promote sleep. If special hypnotic drugs are required, the bromides or paraldehyde will be found safer than veronal or the other members of its group.

If the paralysis is very extensive and the respiratory muscles are involved great care must be taken to prevent the patient contracting bronchitis, or any form of pulmonary disease, which will certainly prove fatal.

In such cases the administration of strychnine hypodermically, combined with atropine, will be indicated, together with the administration of oxygen. Artificial respiration may sometimes be needed, but the case is then desperate.

If cardiac failure threaten, stimulants, strychnine and digitalis must be used.

Ataxia, which is a marked feature in some cases, must be treated by carefully devised exercises as, for instance, those recommended by Fraenkel.

After the acute stage is over, massage, passive movements and electrical treatment should be employed as already described; and the patient placed on a nutritious diet. Malt and cod-liver oil are at this stage often very useful.

2. **Acute Toxic Polyneuritis.**—This disease is characterised by the rapid onset of acute and widespread motor paralysis, with or without definite sensory disturbances. The cause of the condition can rarely be determined, and the treatment is symptomatic and similar in most respects to that already described.

The administration of strychnine and atropine are more likely to be called for than in ordinary cases of multiple peripheral neuritis.

The strength must be maintained by frequent administration of liquid food, and alcohol should be given when necessary. If the patient survives the acute stage, recovery is nearly always complete.

Tumours of Nerves.—These include the various kinds of neuro-fibromata, malignant neuromata and amputation neuromata.

The treatment of the innocent varieties is purely symptomatic, but the malignant type requires excision or amputation of a limb at the earliest possible moment.

Amputation neuromata, if possible, should be excised.

Local Neuritis.—The etiological factors which underlie this condition must be carefully sought for in any case which presents itself for treat-

ment. Briefly speaking, the causes may be divided into (1) General, (2) Local.

Under the former category come rheumatism, gout, septic absorption, anæmia, tuberculosis, syphilis, and indeed practically all the conditions mentioned as etiological factors in connection with peripheral neuritis.

Included among local causes we find arthritis occupying a prominent position, followed by trauma, and pressure on nerves whether by new growths or some other cause.

When found, the primary cause of the nerve disorder must be treated *secundum artem.*

In the treatment of the neuritic condition the same *general principles* hold good that have been mentioned as guiding treatment in multiple peripheral neuritis. One or two forms of local neuritis, however, require separate consideration.

1. **Brachial Neuritis.**—The chief characteristics of this complaint are pain in the arm and round the shoulder, increased by exertion or movement of the limb, and usually accompanied by subjective sensations of tingling and numbness in the fingers. It occurs more often in women than men.

The cause is often very difficult, sometimes impossible to determine.

Arthritis of the shoulder joint is a common factor in producing brachial neuritis, and requires appropriate treatment, *q. v.* As the joint condition improves the neuritic symptoms will also subside.

Cervical ribs, especially in women, are also a common cause of brachial neuritis, and must be excluded by X-ray photographs. If they are present and are causing severe pain or muscular atrophy excision of the rib is the appropriate treatment.

The majority of the cases, however, appear of rheumatic or gouty origin, chiefly the former, but in a proportion of cases, especially in middle-aged or older people, arterio-sclerosis, involving the vasa nervorum, would appear to be the cause of the acroparæsthesiæ complained of.

Heart disease and thoracic aneurysm, especially when involving the aortic arch and its branches, sometimes causes much brachial pain and must be carefully excluded.

With regard to the treatment of brachial neuritis proper, rest and warmth are two essential aids to relief of pain. The former may be secured by using a sling, pinned so that the weight of the limb falls on the *opposite* shoulder to that of the arm involved. Warmth may be applied either as radiant heat, or if this is not available, hot fomentations, followed by the application of thermogene wool, secured by means of a light bandage, often gives great relief. So, too, does the ordinary flat-iron heated and applied over brown paper.

Ionisation is often of great value, the drugs introduced being sodium salicylate or tincture of iodine (vide *Peripheral Neuritis*).

With regard to general treatment, that for gout and rheumatism must be undertaken (*q. v.*) if these are found to be the exciting causes. Such treatment, together with local treatment for the affected limb, can be well carried out at the various English watering-places, Harrogate, Llandrindod, Droitwich and Buxton or Bath. The latter is more suited to elderly people than some of the others.

The bowels require careful regulation, any tendency to constipation must be effectively overcome. The urine must be examined to determine the presence of any latent bacterial infection, and the teeth must be examined for pyorrhœa and treated if this is present. Any other possible source of septic absorption must be excluded. There is no doubt that in a certain number of cases the removal of such a focus will be followed by rapid cure of the neuritis.

With regard to drugs, salicylate of soda, given alone by the mouth, is rarely, in my experience, of much value. Aspirin, 10 or 15 gr., t. i. d. gives more relief.

I have often found the following mixture very effective—

Sod. Salicylatis gr. x
Sod. Iodidi gr. v
Caffeine Citratis gr. v
Sp. Am. Aromat. ♏ xx
Aq. Chloroformi ad ℥ fs.

Sodium bromide may sometimes be substituted for the salicylate with advantage, as may also phenazone in 5 gr. doses.

The Syrup Ferri Iodidi in drachm doses is often of much use, and in the arterio-sclerotic cases Pot. Iod. 5 to 10 gr., with Liq. Trinitrini 1 min., may be given three times daily.

Locally, the application of methyl salicylate in olive oil, or a liniment composed of Lin. Belladonnæ, two parts, Lin. Chloroformi, four parts, often gives relief.

Blistering is sometimes of value in the chronic cases, blisters about the size of a florin being applied over the spine and down the affected limb over the painful areas.

2. **Sciatica.**—In no disease is it of greater importance to make sure of the diagnosis, because numerous more or less serious disorders may give rise to sciatic pain as a symptom.

Arthritis of the hip joint is among the most frequent of these, but of more serious import are pelvic or cauda equina tumours, and tabes dorsalis.

Having established the diagnosis of a pure sciatica, treatment must be conducted on the general lines already laid down in considering neuritis (*q. v.*).

Very slight cases may be treated by the administration of aspirin in 10 or 15 gr. doses, but the more severe cases require careful and often prolonged treatment. It is of great importance to treat a severe case, from the first, by rest in bed.

Rest to the limb may be secured either by the application of a long splint, or by the use of sand-bags, if the splint is not well borne. Warmth may be obtained by the application of thermogene wool to the limb, securing it with a light bandage, and by the application, from time to time, of the hot flat-iron through lint or brown paper.

In the early and most acute stages of the disease massage is contra-indicated.

It is most important to treat any constipation which may be present, as there is no doubt that the sciatica is aggravated by this condition.

The *drugs* recommended for brachial neuritis are of value here.

In the more chronic cases sodium iodide may be administered to the limit of tolerance often with considerable advantage.

Electrical treatment may be given on exactly similar lines to those mentioned under neuritis (*q. v.*), but in obstinate cases good results are recorded from the use of X-rays.

Local Treatment.—Should the methods indicated fail to give relief, local treatment is sometimes very effective.

The application of the Pacquelin cautery is useful as a counter-irritant, but the best results have been obtained from injections within the sheath of the nerve (Lange).

The technique is briefly as follows—

The nerve is attacked either as it emerges through the sciatic notch, or between the tuber ischii and great trochanter. A hollow needle is used and the nerve transfixed at one or other of these levels. An anæsthetic cannot be given, as the patient has to say when the nerve is reached by the needle, an occurrence which is readily recognised. After the needle has entered the nerve 2 c.c. of 2 per cent. eucaine are infiltrated into the nerve, followed shortly by the injection of 100 c.c. of sterilised 0·9 per cent. saline at temperature of 100° F. The injections may have to be repeated on two or three occasions, but the relief obtained is often very striking. It is not particularly easy to hit off the nerve, and some practice is required to do so.

Surgical intervention for stretching the nerve is not to be recommended, as occasionally serious and permanent damage results from this procedure, and the same may be said of alcohol injections within the nerve sheath.

Climatic treatment is sometimes necessary, a warm dry climate being most suitable for patients with this disease.

Nerve Injuries.—When a nerve is divided as the result of an open wound, the cut ends must be found and united at once (primary suture). If this is done, good results may be anticipated.

Injuries to the Brachial Plexus, Birth Palsies.—Where there is no open wound, as, for instance, in cases of brachial plexus injury from trauma, whether the result of falls, blows, wrenching or pressure, expectant treatment should be adopted at first. In the early stages it is impossible to decide with certainty whether the nerve has been torn across or only bruised. Even if the bruising has been so severe as to cause degeneration of nerve fibres, if its continuity has not been interrupted, regeneration may take place.

Treatment, therefore, should consist in supporting the paralysed muscles, and maintaining their nutrition by massage and electricity applied in accordance with rules laid down under *Neuritis* (*q. v.*).

Should no improvement take place, or only partial recovery occur, as the result of three or four months' treatment on these lines, the advisability of surgical intervention must be considered. If operation is undertaken it may be necessary to free the nerve from adhesions or scar tissue, if its continuity has not been interrupted. To test this the proximal part of the nerve trunk should be stimulated by sterile electrodes. Should muscular response occur satisfactorily, the nerve may be left, but should no adequate response occur, nerve anastomosis may be necessary, or secondary nerve suture following excision of scar tissue in the damaged nerve trunk. C. M. H. H.

Herpes Zoster

In this disease there is usually a period before the characteristic symptom appears, during which pain, sometimes severe, occurs, and the patient is often febrile.

The disease at this stage is not to be diagnosed with certainty, and treatment must be purely symptomatic.

Abortive treatment is probably never successful, though applications of alcohol, ichthyol or resorcin have been recommended.

Treatment of the Acute Condition.—The disease, in many cases at all events, appears to be of an infectious nature. For this reason it is well to isolate the patient, most commonly a child, from other children who may be in the house. The bowels should be opened, and if there is fever, a simple febrifuge ordered.

For the vesicles, simple painting with flexile collodion is as good as anything, or a powder of zinc oxide and starch may be thickly dusted on, and covered with dry wool and a light bandage.

If there is much pain, powdered opium may be added, or an ointment applied, composed of

Ung. Boracis to which cocaine (5 gr. ad 1 oz.) ıas been added.

When the vesicles have dried, zinc ichthyol salve muslin, as recommended by Jamieson, nay be applied, as it seems to promote healing.

Treatment by blisters applied to the spine, or over the painful areas, does nothing but harm, and should be avoided.

In **Herpes Ophthalmicus** the eye must be kept protected by a pad, and frequently washed with Lotio Boracis (10 gr. ad 1 oz.) to which zinc sulphate (1 gr. ad 1 oz.) has been added.

In cases in which iritis supervenes, the in-stillation of atropine will be indicated.

The eruption on the mucous membrane of the nouth should be treated by an antiseptic gargle, uch as Garg. Pot. Chlor. (10 gr. ad 1 oz.), or by Glycothymoline.

After-Treatment.—In the majority of cases the eruption disappears in a fortnight or so, and eaves no after-effects. In patients of an advanced age and weakly disposition, neuralgia, ometimes exceedingly severe, may occur as a equel. In the worst cases morphia has been equired to control this, but the milder forms nay be relieved by aspirin, antipyrine or affeine, given in the form of a powder con-aining 5 gr. each of the first two to 2½ of the atter. At the same time the general health nust be attended to, and the ordinary measures f feeding up, change of air, and so on adopted. Quinine and iron may be given as tonics, but rsenic must be used with care, as its exhibition as been said to cause herpes (often bilateral) n elderly subjects.

Local treatment by electricity may prove seful (vide *Neuritis*). Herpes in the cranial egion associated with facial palsy, requires no pecial treatment beyond that described.

C. M. H. H.

NEURALGIA

The term neuralgia, or nerve pain, in its teral application includes all forms of pain ue to nerve injury, inflammation or other auses. Used in its special sense the term euralgia would indicate pains felt in the area f a nerve supply, the nerves of which are ealthy and normal. Sometimes such neuralgia idiopathic, being an expression of a current eurosis, or it may be of toxic origin, some articular state of health of the individual such s anæmia, the monthly period or gestation, right's disease or diabetes being the exciting ause. Frequently neuralgia is reflected along ealthy nerve trunks from an irritant focus on ne small branch of the main nerve; common xamples of this form are afforded by dental euralgia, in which a septic neuritis affecting ne nerve filaments supplying the pulp of a ngle tooth may light up furious neuralgia affecting the whole territory of the mandibular and maxillary nerves, or, indeed, of the whole trigeminal distribution on the same side of the head, the pain, indeed, sometimes radiating beyond into the cervical branches on the neck and back of the head, and even into the arm itself.

Idiopathic neuralgia is essentially a disease of adult life, never affecting children except in the form of migraine. Almost any area or nerve may be the subject of this disease, which may occur in the form of lancinating, so-called "neuralgic" pains, or of boring, cutting pain in one particular spot. The nerve territory which suffers most severely and most frequently from neuralgia is that of the trigeminal nerve, and obstinate pain in one or more divisions of this nerve is known as trifacial or trigeminal neuralgia. The most frequent cause of pain in this area is the teeth, and persistent neuralgic pain referred to either the maxilla or mandible from the region of the ear should never be assumed to be idiopathic or of the nature of tic douloureux without the most careful ex-amination of the teeth on that side. Dental neuralgia may be referred from the mandible to the maxilla, or vice versa, and, though the pain may indeed spread into the neck or over the whole of the same side of the head, it is never referred to the opposite side. Thus, a carious tooth in the mandible may sometimes give rise to pain felt only in the upper jaw on the same side, but it will never cause pain on the oppo-site side of the face. Moreover, supra-orbital neuralgia occurring alone is never due to dental causes.

Pyorrhœa, or chronic suppuration of the gums around the roots of the teeth, may be a cause of persistent neuralgia of the face and head, and severe dental neuralgia radiating along one or other jaw and occurring in spasms, especially with eating or talking, may be due to congestion of the pulp inside the apparently sound tooth. This congestion is the preliminary to necrosis of the pulp and nerve filaments supplying the tooth, so that later the tooth becomes "dead." During the dying stage in the process of con-gestion the tooth will be especially sensitive to heat, and by this means the offending tooth can be localised. Again, in other cases violent neuralgia may be due to periodontal inflamma-tion, usually in a tooth which has been filled, particularly in a recent filling of the roots; in this case the nerve will not be especially sensitive to heat or cold, but will be very sensitive to pressure, as when closing the jaws if it touches an opposing tooth; extraction of the tooth is the only safe remedy in the latter event, as suppuration with necrosis of the jaw may other-wise follow, which, in the upper jaw, may lead to ocular and retro-ocular inflammation, cavernous

sinus thrombosis, or cerebral abscess and death. Again, an impacted tooth, or a lower wisdom tooth, by pressing upon the inferior alveolar nerve, which runs close beside its roots, may be the cause of an intractable though variable neuralgia. An X-ray photograph of the jaw should be taken in every doubtful case in order to exclude the possibility of this and other causes of neuralgia, such as buried stumps, exostoses and the like.

Next to the teeth the maxillary antrum and frontal sinuses are of importance, and severe neuralgia in the cheek, with tenderness and hyperæsthesia below the eye and along the side of the nose, may be set up by acute suppuration within the maxillary antrum. The best means of recognising this condition is by transillumination, in which a small electric bulb is held within the mouth with the lips closed tightly over the stem, the room being darkened. If the cavity is filled with pus a dark shadow replaces the brilliant crimson light which, normally, should show below the eye and over the prominence of the cheek. When making such an examination by transillumination it is, of course, necessary to remove any dentures or tooth plates, which would otherwise throw dark shadows which may be mistaken for pus. Accompanying it, or resulting from a running cold in the head, there may be great supra-orbital tenderness, with heavy aching pain over the eyebrow, due to frontal sinus congestion.

True trigeminal neuralgia, or tic douloureux, almost invariably affects either the second or third divisions of the nerve, sometimes both divisions, on one side only; very rarely is this disease bilateral. This disease has no apparent relationship to dental causes, and extraction of the teeth is of no value; indeed, tic douloureux may commence many years after all the teeth have been lost. It has been ascribed to various causes, such as disease of the Gasserian ganglion, or epileptiform discharges in the nucleus of the trigeminal nerve; more probably, if not certainly, it is due to septic ascending neuritis of the dental nerve filaments, originating either from an antecedent dental caries or from pyorrhœa, the septic focus persisting in the nerve filament even after the loss of the tooth

The paroxysms of pain in tic douloureux closely resemble those sometimes seen in true dental neuralgia; they may be of all degrees of severity, and occur often in spasms lasting a few seconds to many minutes. The pain is often described as of a twisting, darting character, like hot needles being bored into the flesh; the paroxysms are usually started by the act of eating or talking, or even a light touch upon the chin or lip or nose may induce a furious attack of pain, though immediately the attack is over, and for a few minutes afterwards, no stimulus or pressure may be able to provoke it. Weather, with the exception of cold winds, makes very little difference, the pain being often as bad in hot as in cold weather. Intervals of complete freedom from all pain may occur for weeks or even months, though as years go by these intervals become shorter. True trigeminal neuralgia is a disease which persists for the rest of the patient's life unless operative treatment of the nerves or Gasserian ganglion is undertaken. Drug treatment is of little value in the majority of cases, though in a few tincture of gelsemium, in 20 or 30 min. doses, may relieve; butyl chloral hydrate is probably of less value. Electrical treatment more often than not increases the pain. Neurectomy used frequently to be practised, and complete relief has often been obtained for intervals varying from three or four months to three or four years, by section of the inferior dental nerve or of the infraorbital nerve, according to circumstances.

Recurrence is, however, inevitable, and secondary neurectomy is unsatisfactory, even if possible. Excision of the Gasserian ganglion was, therefore, devised and practised by the intracranial route, with resulting complete cure of the pain, in this case permanent, but at the expense of anæsthesia of the front half of the head and a risk of corneal destruction from ulceration. A newer and extremely satisfactory treatment is to inject the nerve trunk of the maxillary or mandibular division, or both, according to the distribution of the neuralgia, with strong alcohol at the foramen rotundum or foramen ovale respectively. This is by no means an easy operation, and should not be undertaken by any one who has not previously practised the method thoroughly upon the dead body; even then considerable experience of the method is necessary before the operator is sufficiently familiar with the difficulties and variations that may be required to insure the probability of his finding and injecting the nerve correctly. Chloroform anæsthesia may be used, and, unless the operator is thoroughly familiar with the method, this is perhaps a better plan. Better results, however, will be obtained when the patient is sufficiently conscious to feel a tingling sensation when the needle reaches the nerve, and to answer to tests of sensibility of the skin in the area of the nerve injected. A preliminary injection of morphia, $\frac{1}{3}$ gr., with hyoscine hydrobromide, $\frac{1}{150}$ gr., given hypodermically twenty minutes before the operation is begun, is sufficient to quiet a nervous patient, and makes the injection process easier, while the patient is able to answer all questions.

To reach the foramen rotundum of the second division a 3-inch needle, with a short point and a stylet, should be pushed through the outside of the cheek beneath the malar bone and passing

n front of the coronoid process of the mandible nd behind the maxilla, upwards and slightly ackwards in the direction of the external terygoid plate. The point for insertion of the eedle may usually be felt by palpating with the nger the under surface of the malar bone and he front edge of the coronoid process, this point eing usually about 2¼ inches (58 mm.) in front f the middle of the external auditory meatus. 'he needle should be pushed in the line of the scending orbital process of the malar bone, at n angle of 40 degrees, *i. e.* slightly less than half right angle with the horizontal plane. At a epth of about 2 inches the external pterygoid late should be struck, and then with gentle novements, the point of the needle is guided orward until it slips in front of the anterior order of the pterygoid plate, the needle being ently pushed inwards in the same line for nother ¼ inch, when the maxillary nerve hould be reached at its emergence from the oramen rotundum; this will be indicated by the atient suddenly complaining of a twinge in the heek, side of nose, and upper lip. When that the case the needle must be gently pressed wards another one or two millimetres, the ylet removed from the needle, and the syringe, ontaining 5 per cent. novocain sterile solution, tted on, taking care to hold the needle absolutely steady. Five to seven min. (0·3 c.c.) the novocain solution is then injected, when e patient instantly feels a sensation of a spray the face. Then, after waiting a full minute, e syringe is gently disengaged from the needle d another syringe, containing 90 per cent. cohol, is fitted in its place, taking the utmost re to hold the needle steady, then 5 or 6 min. the alcohol is slowly injected, and, after a few conds, the patient experiences a certain degree burning sensation in the cheek, nose and lip. fter another minute the skin of the upper lip tested with a pin, and if the nerve has been roperly injected there will now be found well-arked anæsthesia. Then, a few drops at a me, more alcohol should be injected until 1 c.c. 8 min.) has been used, the whole territory of e maxillary nerve being now deeply anæs-etic. The needle is now withdrawn slowly d carefully, and after a few minutes' pressure ith a swab upon the site of puncture, to stop ozing, a small collodion dressing should be pplied.

The chief difficulty that is met with in this jection is that it may be impossible to pass e needle in front of the coronoid process d through the pterygo-maxillary fissure on count of the backward bulge of the maxilla. When this is the case the needle must be inserted ehind the coronoid process, about ½ inch below e lower border of the zygoma, and must be en directed slightly upwards and backwards, when the nerve may be struck slightly in front of the foramen rotundum. There is considerable risk of hæmatoma being produced by this injection, particularly by the anterior route, owing to injury of the internal maxillary vessels.

To reach the foramen ovale the tubercle on the lower border of the zygoma should be marked and a vertical line drawn through it, as the plane drawn through this line at right angles to the cheek passes through the foramen ovale. The tubercle is on the average exactly 1 inch (25 mm.) in front of the middle of the external auditory meatus, and the foramen ovale lies at a depth varying from 42 mm. in thin, narrow-faced subjects, to 64 mm. in stout, square-headed people. A 3-inch needle should be used and pushed through the outside of the cheek a few millimetres below the lower border of the zygoma and slightly in front of the vertical line already drawn. The needle is pushed in a direction very slightly backwards and upwards, in order to reach the plane already described at the required depth. When the nerve is struck a twinge may be complained of in the chin or lower jaw, when novocain, followed by 90 per cent. alcohol, should be injected in the manner already described. In many cases, however, the twinge is not referred along the distribution of the nerve, but the pain is felt only locally and at the back of the jaw. This is often so, even when the nerve has been properly punctured by the needle, and, therefore, if such a pain is complained of, or if the patient clearly flinches when the needle is presumably in the region of the foramen, two or three drops of novocain solution, followed by 3 or 4 min. of alcohol, should be injected, and after waiting for a full minute, keeping the needle steady, the chin and lower lip should be tested for anæsthesia with a pin. If distinct anæsthesia is present the needle is rightly placed, and more alcohol should slowly be injected. If, however, no anæsthesia is found on testing, then the needle must be gently partially withdrawn a few millimetres, and re-inserted in slightly different directions until the required result is obtained. A very large proportion, probably more than 50 per cent., of patients who are treated by this method fail to complain of pain along the distribution of the nerve when it is struck by the needle, and the only proof that the nerve has been correctly injected is the rapid appearance of complete anæsthesia of the whole area of distribution of the third division of the nerve, lower lip, half of tongue, a strip on the outside of the cheek, etc. There is also motor paresis of the masseter and temporal muscles on that side, and when there is total anæsthesia of the half of the tongue there will also be total loss of taste over the same area.

If deep anæsthesia is obtained in the territory

of the injected nerve, as should be the case if the nerve is properly struck, painful spasms usually cease from that moment, and complete freedom from the neuralgia will ensue for periods varying from twelve months to four years or more. When recurrence of the pain occurs the same treatment can be repeated with equal success, there being no scar or other deformity to interfere, as is the case after cutting operations with the knife.

Occasionally neuralgia affects the region of the ear, both in front and behind, and in the depths of the meatus, due to lesions of the facial nerve in the neighbourhood of the genicular ganglion, and it may be accompanied by herpetic eruptions on the tympanic membrane and posterior wall of the meatus and also on the back of the pinna. Such neuralgia often accompanies a Bell's palsy, and very occasionally may be severe and last for many weeks.

Neuralgias in the limbs, brachial and sciatic neuralgias, may be evidence of a brachial or sciatic neuritis, or they may be toxæmic in origin, *e. g.* gouty or diabetic, or they may be associated with radiating pains and tender points around the shoulder blades and back or lumbo-sacral region, due to **fibrositis.** This consists of a subacute inflammation of the fibrous tissue forming the intermuscular septa and fibrous aponeuroses attaching the muscles to the shoulder and pelvic girdles of the vertebral column, and may originate as an expression of a gouty or rheumatic process, a common instance of the latter being lumbago. When affecting the region of the shoulder, pain may be complained of between the shoulders and down the vertical border of the scapula, often radiating into the neck and back of head, and down the arm as far as the insertion of the deltoid, or in a few cases even reaching to the wrists and fingers. Acutely tender points may be found on pressure, usually between the vertebral border of the scapula and middle line; on pressing on these with the finger or with the blunt end of a pencil, sharp pain may be complained of as though a needle had been run in. These points should be marked, and if the same points are found persistently tender day after day, an excellent treatment is to inject each with 0·5 c.c. alcohol, using a fine needle, 2 inches (25 mm.) in length, and inserting it vertically over the tender point and pushing it down to the bone of rib or vertebra; if 5 min. of 5 per cent. novocain solution is injected before the alcohol the process is scarcely painful, but in many cases remarkable relief from intolerable pain may be secured. Not more than two such tender points should be injected with alcohol at one sitting, and an interval of two days should be allowed before the treatment is continued. When the tenderness is more diffuse or absent, local injection with alcohol is contra-indicated and other treatment must be tried, such as cataphoresis, or ionic medication with salicylate of soda or iodine, radiant heat baths, hot saline packs, menthol and methyl salicylate liniments and later in the chronic stage, deep massage. Internal treatment by aspirin, colchicum and lithia may also be of service.

W. H.

TREATMENT OF MENTAL DISORDERS

Preliminary.—The treatment of mental disorders has been influenced by two well-marked doctrines, the one tending to postulate that the healthy condition of the mind depends upon the healthy condition of the body and the other maintaining that the body or mind, or both body and mind, of the patient have become possessed by some malign intruder. The first doctrine was formulated by Hippocrates, who described "determinations of humour" as the occasion of madness, and he has been followed by all those who, since his time, have followed the scientific methods of observation and experimentation. Aretæus asserted that the cause of madness was seated in the head and hypochondriac region, the process sometimes commencing in both regions together and the one sometimes imparting it to the other. Paulus Ægineta wrote that in melancholy the brain is sometimes primarily affected and at other times is altered in sympathy with the rest of the body, a position which might well be taken by a modern pathologist and the one which will in the main govern the therapeutic notions submitted in this article. It is important to bear in mind that as in medicine in general so in psychological medicine in particular there is a feeling abroad that the study of morbid structure has almost reached its fruitful limits, that a diseased structure may at least as well be conceived as following upon diseased function as may disordered function be conceived as following upon diseased structure, and that the minds of students of medicine may most usefully be turned in the direction of the investigation of the beginnings of morbid function. It is reasonable to suppose that the nervous system, including brain, spinal medulla, peripheral nerves and sympathetic system, is associated with the group of phenomena con-

stituting that which we know as feeling, perception, memory, reason, judgment and will, or, using one word, the mind. Some have held that thought is the secretion of the brain and others that the brain is but the very humble servant of an extra-corporeal entity, and no controversy appears further from settlement than that which has for its central problem the connection of the brain with the mind. It is certainly not for us to attempt here any solution, and we only mention the matter inasmuch as it is of importance to remember that while many physical agents may be assigned as causes of insanity in so far as they produce structural alterations, it is also becoming increasingly apparent that stress, worry, an undue amount of emotion, or a wrong quality of emotion, or a wrong treatment of normal emotion, may so affect the proper carrying on of the functions of the mind, that the phenomena of insanity may occur. Hope of betterment in the treatment of the insane lies in a study of the causes of mental ill-health, and while it is of the utmost importance that every effort should be made to discover associated somatic disease, there should also be an endeavour to discover whether in the patient's mental life there have been circumstances which might also have acted as causative factors of insane manifestations.

The more pronounced symptoms of insanity are so extremely unpleasant and so often are a cause of offence to those sane individuals with whom the patient may come in contact, that it is not altogether surprising that they have been ascribed to the malign influence of some devil or evil spirit that has taken possession of the unfortunate sufferer. In times when all the phenomena of life were regarded as the direct handiwork of supernatural agencies, either good or bad, bodily and mental ills were also attributed to such agencies, and the annals of sorcery are full of stories indicating to us of a later generation, and, as we hope, of a fuller knowledge, the diseased mental and somatic states of many wretched persons whose symptoms were regarded as sins and who were in consequence tortured and done to death with horrible barbarity. The theory of "possession" is not, however, to be ignored, inasmuch, crude as it may be, it occupies nakedly or in some modified form the popular conception of insanity and the treatment proper to it. Its trail can be followed in the word lunatic, and in the idea that a lunatic is one who has to be "locked up" in a building scarcely distinguishable from a prison, to be placed in a padded "cell" and to be "captured" if he "escapes." The statute book has in large measure been modified in recent times by this same conception, and the modern Lunacy Law is based on the principles, firstly, that an insane person must be deprived of liberty, and secondly, that the person of the sane individual must be scrupulously defended, lest the almost impossible should happen and he should be haled off to a lunatic asylum by force or fraud. Such are the guiding motives of the present law, and from it seems to be excluded all idea that the insane individual is ill and is therefore to be treated as best modern science and art can treat him. This is a matter of practical importance, for the medical practitioner has always to bear in mind that his treatment of a given case must be influenced by consideration of an absurd law. If the friends of a patient presenting mental symptoms do not desire certification, it is only by evasion of the law that the patient can be treated by those competent in knowledge and experience. In the Lunacy Act of 1890 we read in Section 316: "Every person who, except under the provisions of this Act, receives or detains a lunatic, in an institution for lunatics, or for payment takes charge of, receives to board or lodge, or detains a lunatic or alleged lunatic in an unlicensed house, shall be guilty of a misdemeanour and in the latter case shall also be liable to a penalty not exceeding fifty pounds." The provisions of the Act referred to are those which concern certification, and it is only under them that, according to the law, the patient can be removed from home surroundings, which are admittedly the worst possible for him, and be placed where he can be properly looked after. It is certainly to be hoped that some day or other the law may be so framed that its first concern will be with the mentally afflicted person as a patient and that only secondarily will it concern itself with those very rare and indeed almost impossible cases in which it is alleged that sane persons are improperly detained. When this happy consummation has been reached it may be expected that patients will submit themselves to treatment at an earlier stage of their affections and at a time when our art can do more for them than at later stages when irreparable damage has been done, and that they will no longer be deterred by knowing that an admission on their part that they have mental symptoms will brand them with the stigma of certification. Rightly or wrongly, certification is now regarded as a last resort, and as a measure by all means to be avoided. It immediately follows upon this widely-spread feeling that mental symptoms are disregarded, belittled and concealed, and if eventually they have to be disclosed, are ascribed to "nerves." It is in this way that time of essential importance is too often wasted and that it is only in an advanced stage of disease that a patient is

brought under treatment. In the account of the treatment of mental disorders which follows, we propose to deal with such phases of the affections in question as come within the purview of the practitioner, whether he decides only to be responsible for the initial stages of the illness or to take the responsibility of seeing it right through.

From what has already been written, it will be clear that to deal with symptoms at the earliest moment of their appearance is of great importance, and we would now further lay stress upon anticipating the occurrence of symptoms by the proper education of predisposed individuals and the regularisation of their lives. Bearing in mind the events which so often immediately precede attacks of mental disorder and which are not uncommonly erected into "causes of insanity," the neuropathic individual should be especially warned against excesses of all kinds. An amount of alcohol, of venery, of work, of worry, or of the toxins of various infective processes which would do but little harm to a person not predisposed to nervous and mental disease, may, in the predisposed person, result in serious, if not complete, disablement. The idea of regular hours for work, for exercise, for food and for sleep should be inculcated from the earliest years, while such a profession should be selected for the neurotic individual as will put the smallest amount of strain upon his nervous system. As a rule, it may be laid down that outdoor occupations are better than those which keep the patient at an office desk, or involve many hours in a shop or an office varied only by hurried journeys from and to the suburbs. Working late at night is particularly harmful to the neurotic, and by sooner or later producing insomnia may prove a determining cause of a breakdown. Particular attention should be paid to the body weight, for it is very frequently the case that its diminution is the first sign of the approach of mental symptoms. While it is highly undesirable that a predisposed person should be made into a valetudinarian, it is yet important from the earliest years to instil such an amount of regard for health as is suggested above. If such education is in fact commenced very early, good habits will be formed and will be automatic long before the individual shows that care for his health which comes of melancholy experience, and which may so easily absorb an excessive amount of the care and attention of him who has to learn late and who has no basis of good habit upon which automatically to act. While a proper amount of care for the bodily health is being taught from the earliest years, the education of the character must not be neglected. Education in general knowledge, in the classics, in science and in the arts should never be pressed in the neurotic child or young person, and progress should be restrained rather than accelerated, while all signs of precocity of genius in any one direction are to be regarded with extreme suspicion. While we believe this to be true of the components of education which we have mentioned, and which too often are apparently held to be the chief or the only ones worthy of serious consideration, we are convinced that it is to the neglect of the education of what is known as character that many of the abnormal manifestations of mental morbidity are due. The child who is never taught to control himself and to bring his body into subjection, has the makings of the man who cannot restrain himself from excesses in all directions and especially in those which constitute factors in the causation of mental disease. The child whose smallest whim is always gratified and who cries and makes himself a nuisance if he does not at once get what he wants, is likely to become the man who can ill bear being thwarted either by his fellows or by his circumstances, whose temper is hasty and capricious, who worries over absurd trifles and is ill-fitted to stand up to the more serious buffets which are the natural lot of mankind. Above all, the child whose world has been egocentric and who has been taught by example and precept to pay but scant regard to the feelings and the good of his neighbours, is likely in adult life, when the rewards of the pleasures of the senses are found to be of less value than had been supposed, to suffer from an ennui and want of purpose in life which dispose to a depressed condition of affectivity. So far then as prophylaxis is concerned, we would urge that in the neurotically predisposed person particular care should be taken in his educational preparation for life and that he should early learn that a lowered standard of physical health is likely to end in mental or nervous disorder. In the case of the individual who has not been recognised as neurotic, or who has become so owing to adventitious causes, the work of the physician is harder. Habits of thought and of body have been formed and are so set that it is difficult to modify them, but nevertheless efforts must be made to regularise the patient's life from the physical standpoint and to endeavour to induce him to adopt that which appears to his adviser to be the intellectual attitude proper to his condition. This matter will be further dealt with when we come to consider the methods of psycho-therapy. It is too often the case that symptoms are so pronounced by the time advice is sought, that the patient is already in a bad state of physical health, his weight is far below that which is normal

to him, and, although he may show superficial signs of energy, he is in an exhausted and asthenic condition, while his mental state may be such that he is quite unable properly to look after himself. The commonest symptoms with which we have to deal, among those who may be definitely classed as mental patients, exhibit themselves in states of excitement and states of depression, and it is first of all to the treatment of these conditions that we shall address ourselves, subsequently dealing with other manifestations of mental disorder.

Mania.—Whether a patient comes under observation at a stage when the symptoms are slight and there is but little mental excitement added to the loss of weight and sleep, which has almost invariably preceded the psychic disturbance; or whether, as is too often the case, mental disorder has eventuated in conduct which by its unseemliness or violence has attracted attention, treatment is the same. It may, of course, be necessary that treatment should be carried out at an asylum, or it may be possible at the patient's home, or in a nursing home, or in a doctor's house, and the problem as to where the patient should be, will now be considered. It is in but a few cases that a patient can be efficiently treated at home, for, in the first place, space is usually wanting. The patient should be in some isolated part of the building where he is away from those sights and sounds which are associated with the ideas of home and near relations, and which are almost invariably of bad effect and are the cause of agitation and worry. If the patient possesses an insight into his state and is aware that his mind is deranged and that his conduct is strange and possibly ridiculous, he dislikes exposing himself in this state to the inspection of relations and friends. If, on the other hand, he has no insight, he may re-act emotionally to the presence of his friends in a way which is exciting and bad for him and disagreeable to them. But, whatever the explanation, experience teaches us that the presence of friends seldom has a beneficial effect when acute symptoms are present, and that, on the other hand, it has very frequently an effect which is bad. It must further be remembered that relations and friends are mostly ignorant of the symptoms of unsoundness of mind and of therapeutic indications, though they not infrequently have erroneous ideas of the methods of treatment which should be pursued and zealously desire to translate them into practice. In addition then to the effect upon the patient the increased difficulty of properly carrying on treatment must be borne in mind. It is very largely for these reasons that it is, in the majority of cases, desirable that patients should be treated away from their own homes, where not only is it difficult to prevent the meeting of the patient and his relations, but where he is less likely to regard himself as under treatment than he might if he were elsewhere. If then it is thought inadvisable to keep the patient at home, the next point to be considered is whether he can be looked after in a private house other than his own, or whether he should go to an asylum. In the event of the patient being extremely noisy, it is probable that an asylum will be indicated, since such a patient is too disturbing for other inmates in a private house. If a patient is very violent, he can of course be managed with a sufficiently large posse of nurses, but to keep a large number of persons constantly ready to cope with emergencies is naturally so expensive that it can but rarely be undertaken, and in such cases it is usually desirable that the patient should go to an asylum. If, then, the expense of nursing has to be thought of, if the patient is noisy or if he is violent, it is wiser that he should be placed under care in an asylum. If opposite conditions prevail, there is no particular reason why the patient should not be nursed in a private house, provided always that skilled care and attention are available.

Certification.—If certification is decided upon and time is available, the ordinary method may be employed. The process consists in the filling up of five forms, which may be procured at a Law Stationer's, consisting of a petition made by the next-of-kin of the patient, or by some other person, if the next-of-kin is not available; of a statement concerning the patient's age, civil condition and a few other particulars; of two medical certificates filled in by two medical men not in partnership and not within certain degrees of relationship with each other or with the patient or with the person who is appointed to receive the patient into his care; and of an order made by a magistrate authorising the reception of the patient. The legal formulæ are then complete. If time is pressing, a patient may be sent to an asylum or to private care on an urgency order. Such an order is made by the next-of-kin of the patient, or other authorised person, without the intervention of a magistrate, and has only to be accompanied by one medical certificate. When an urgency order has been made and the patient has been sent on its authority to an asylum or to private care, the more cumbrous mode of certification has to be completed within seven days from the date of the order. These are the most commonly employed methods, but the consignment of a patient to an asylum may be effected by a summary reception order made by a judicial authority under the Lunacy Act, by the order

of two commissioners in lunacy and upon inquisition. It is not necessary to do more than to refer to these rare procedures. In Scotland and Ireland the method of certification differs in a few particulars from that obtaining in England.

Wherever the patient is placed, the mode of treatment is the same. The guiding principle should be that the number of stimuli coming from without and impinging upon the patient's sensorium should be reduced to a minimum and that, so far as may be possible, the patient's reactions to stimuli, whether from within or from without, should similarly be limited. Rest should, therefore, be emphatically enjoined, and it is obvious that bed is the best place for a sick person to rest in. In most cases of excitement the patient is far from recognising that he is a sick man at all, and it may be exceedingly difficult to induce him to stay in bed or even to regard himself as ill. In many cases, however, and especially in those which are the least severe, it is possible with tact on the part of the doctor and of the nurses, to induce the patient either to go to bed for days together, or at any rate to pass a larger proportion of his time there. We do not suggest that rest in bed should be enforced in all cases. There are patients to whom this course is of itself the acutest source of irritation, and it is manifest that physically to struggle with a patient to keep him in bed, is not the way to procure for him the greatest amount of rest possible. The room in which it is intended to nurse the patient should be of moderate size and well lighted and ventilated. It should be denuded (except in those cases where the illness is very mild) of all unnecessary ornaments and furniture and especially of such articles as the patient may use as weapons or missiles, or such as he can readily break or otherwise destroy. Beside the possibility of assault upon others, it must be remembered that patients of this class, though not suicidally inclined, are apt impulsively to damage themselves, and, in order to prevent this, ceaseless watching is necessary. This at once introduces us to the question of nursing, a problem always of the greatest difficulty in cases of mental disorder. The success of treatment in the psychoses and neuroses is very largely in the hands of the nurses of the patients. Whereas in illness of a physical character, the skill of a nurse depends more or less on his or her knowledge of certain mechanical duties, and of the skill and facility with which he carries them out, in cases of mental disorder there should be, in addition to mechanical skill, a knowledge of character, tact, patience and a high standard of duty. A course of a few years spent in an institution may turn out a nurse of sufficient mechanical knowledge, but training, however systematised and of however high a standard, will only end in bumptious self-importance unless in the background of the nurse's own mental make-up there lie the qualities which we have enumerated. The number of nurses required varies with the severity of the symptoms of the patient, and it may be laid down that that number is necessary which will ensure the patient being watched continuously. Whatever number above this is required will depend upon whether the patient is violent or not. It is not uncommon to find that some patients will prove very refractory in the hands of one nurse and wholly amenable in the hands of another, the difference in power of the nurses lying much less in physical strength than in the possession of patience, strength of mind and tactfulness. The question of restraint by mechanical means may here be considered. The more such means are avoided the better. In the first place, it is undesirable to induce in the nurses the feeling that when once the patient is mechanically restrained, all is safe and well. This is very apt to lead to laxity in observation and to too early and frequent recourse to the particular mechanism. In the second place mechanical restraint is not unlikely to increase the agitation of the patient and to engender in him a resentment towards those looking after him which may issue in some violent reaction. Mechanical restraint is for the most part a relic of bad old times, and though here and there necessarily employed to prevent the patient from injuring himself or others, should only be thought of when all else fails. Efficient nurses having been selected, so far as is possible, and a suitable régime having been instituted by the physician, it is imperative that patients, for the reasons mentioned above, should not see members of their families or their friends. If the patient has been induced, perhaps only after much persuasion, to remain in bed wholly or for the greater part of the twenty-four hours, it is further desirable, where circumstances permit, that his bed or couch should be placed in the open air, or, if this is not feasible, that it should be so placed that the patient gets as much fresh air as is possible. There is very little doubt that in adopting this practice patients speedily become less excited and that their general nutrition improves. The contrast between the condition of the patient lying in a bed in the open air with that of the patient cooped up in a padded room in which the atmosphere, if not fœtid, is almost necessarily vitiated, is very striking, and will induce all who have remarked it to postpone all thought of the room until the influence of fresh air and rest has been tried and has failed. To see a row

of acute maniacs in bed on a verandah is, one may well write, a refreshing sight when compared with the pitiable memory of the padded or strong room where many of these patients would, under other conditions, have necessarily to be. We hold that if the attention paid to the insane, or at any rate to those among them who are acutely ill, was made at all comparable to that paid to cases of tuberculosis or of the acute infective diseases an immense advance would be made. In every case we would urge that temperature charts be kept, not only for the record of the temperature, but of the various other phenomena which are noted on such charts, for instance the respiration and pulse-rates, the number of times the bowels are opened and the water is passed, the weight of the patient and, indeed, any other detail which may suggest itself. It is perfectly true that this largely increases the work of the nursing staff, and that as asylums and mental hospitals are at present staffed it is impossible : nevertheless the standard is well worth endeavouring to attain. Some sedative hydrotherapeutic measures may here be mentioned. They are unfortunately not frequently practised in this country but are undoubtedly of value in many cases. The warm bath at about 98° F. is the most generally useful and the most appreciated by patients. The patient may be kept in such a bath from half an hour to an hour on the first day, and this period may be rapidly extended until in a few days' time the patient spends many hours in the bath, or indeed may continuously pass his time in it. Patients in baths should be assiduously watched, and if sleep is likely to occur some simple apparatus must be devised to prevent the patient's mouth and nose slipping beneath the surface of the water. Wet packs are also very efficacious in producing an abatement of excitement. The patient is laid upon a blanket below which is a waterproof sheet and is then enveloped in a sheet wrung out with water at about 100° F., while over this is placed a sufficiency of blankets to keep the patient warm. In such a pack a patient may be left for an hour or more. In some cases a similar application on a small scale over the patient's abdomen will result in sedative effects.

The next matter of importance to be considered is the feeding of the patient. Fortunately this does not, as a rule, present much difficulty. At times the patient may be so excited and pre-occupied, that he neglects to take food, but he will usually eat if it is placed before him. Excited patients are very likely insufficiently to masticate their food, and for this reason it is as well to give them purées, minces and other forms of finely-divided food-stuffs. Patients are, as a rule, much thinner than they ought to be by the time that they come under treatment, and the amount of food should therefore be large and of high value. Alcohol should be avoided, and tea and coffee should not be strong. The best drink for such patients is milk, and of it patients should have some three pints a day. The ordinary meals may be given at the usual time, but it is as well to give between them glasses of milk or egg and milk. The question of drugs is the next of importance. Patients are almost always constipated, and it is necessary in the first instance to give a large dose of some purgative. Calomel is perhaps the most convenient, especially in cases where asthenia is but little marked, and may be followed by magnesium or sodium sulphate. When the initial constipation has been overcome, it is well to put the patient on the routine use of some such drug as cascara sagrada or an infusion of senna pods, or one of the natural aperient waters such as Apenta, Hunyadi Janos or Friedrichshall. To abate excitement and to procure sleep are two notable indications in acute mania, and in many cases the various remedial measures suggested above will suffice, but in others, and indeed in the early stages of most, drugs may with advantage be used. It is a pity wholly to rely on drugs and to neglect the more important means at our command, for it is always to be remembered that drugs have toxic properties and that it is a matter of conjecture as to whether these are in operation in all cases or only in those which are exceptional and in which the symptoms of poisoning are marked. Among the most potent drugs may be named hyoscin. The hydrobromide or hydrochloride salts of hyoscin may be given in doses ranging from $\frac{1}{200}-\frac{1}{100}$ gr., and are more likely than any other drug to allay acute excitement. The patient after a dose of hyoscin should, if possible, be induced to lie down and should be watched. A second dose should certainly not be given for at least twelve hours after the first. Morphia is not desirable and may very often produce an opposite effect to the one desired. Opium has, however, proved its value in cases where there has been much physical exhaustion. It should at first be given in small doses and gradually increased until a maximum good effect is produced. Thereafter it should slowly be withdrawn. The bromides in acute excitement are almost useless, but are invaluable in states of sub-acute excitement and when acute excitement is abating. Among the hypnotics the best are sulphonal, veronal, medinal, adalin and paraldehyde. Sulphonal is notably a drug which takes some hours to produce its effect, the amount of time elapsing varying with the

idiosyncrasy of the patient from three to twenty-four hours. The same is true, though to a less extent, of its congeners. Such drugs as these are apt to collect in the intestines, and it is of vital importance that the bowels should be adequately evacuated during the days that they are being administered. As the more pronounced mental symptoms diminish, and as sleep and the bodily condition improves, treatment may very cautiously be relaxed and the patient be allowed up for increasingly long periods, but the return to normal life should be made very slowly and tentatively. When the patient is discharged from care he should be advised to get a change of air and to occupy himself with not too strenuous open-air pursuits before actually returning to work. Where, notwithstanding improvement of bodily health, acute symptoms pass into chronicity, the patient's mode of life will depend for the most part on the more or less strangeness of his conduct : if he is but mildly eccentric there is no particular reason why he should not be housed in a private house, but if, on the other hand, psychic inhibition or dementia are pronounced, it is probably wiser to advise continued residence in an asylum where appropriate pursuits and amusements can be devised for him.

States of Depression.—Whereas we have at present at our command no specifics for the treatment of any form of mental disorder, our methods resolve themselves into dealing with symptoms as they arise and careful attention to the general bodily health. In states of depression the physical health invariably requires considerable care. The patient is constipated, anæmic and sleepless, and has usually lost weight and appetite. It is important at the earliest moment to relieve the state of constipation, and the patient may be given an enema and large doses of castor oil or calomel. When the bowels have been effectually relieved an endeavour should be made to procure a daily action by the means of some aperient. An infusion of senna pods, liquorice powder or Epsom salts are perhaps the drugs most commonly suitable, for the amount of the dose can very readily be varied from day to day, and there is no harm in using them over considerable periods of time. The appetite of the patient is bad for psychic as well as for somatic reasons, but, notwithstanding any foulness of the tongue which may be present and which may appear to be a contra-indication, food should be pressed. A patient who is at all seriously depressed will rarely eat an adequate amount of food if left to himself, and one of the most exacting duties of the nurse and one requiring an infinitude of patience is to induce the patient to eat. In the majority of cases, given time, tact and patience, food can be administered in proper amount, but in a residue it has to be given forcibly by the spoon or the tube. Some patients when they find food in their mouths will swallow, but others will forthwith spit it out, and in the latter case feeding by the nasal or œsophageal tube must be had recourse to. It is as well not to put off forcible feeding too long, for it is undesirable to add the symptoms of starvation to the symptoms from which the patient is already suffering. Feeding by the tube, though unpleasant on the few first occasions, is not painful and patients soon get used to it. The food administered by the tube should consist of milk, eggs and milk, and milk thickened with such articles as Benger's Food, vegetable extracts, Sanatogen, Ovaltine and the like. Feeds should be given, in the event of a total refusal of food, three or four times a day. To those who will eat with persuasion, food should be given at the ordinary meal times, should be easily assimilable and should have a high nutritive value. In between the ordinary meals, glasses of milk or cups of Benger's Food or other similar foodstuffs should be given, and it is especially desirable to give the patient a cup of hot milk or other food just before he is settled for the night, for this not infrequently promotes sleep.

A period of rest in bed rarely comes amiss in the treatment of a depressed patient, and indeed is distinctly indicated where there are signs of exhaustion and much loss of weight. The methods by which it has in the past been sought to distract the mind of the patient or by induced physical fatigue to improve his mental state have, for the most part, ceased to be practised, but it is not improbable that it will be found that before the patient has come under treatment he has been treated by well-meaning relatives by some such methods. The signs and symptoms which now suggest to the medical mind the need for rest of the highest psychic functions are unfortunately those which suggest to the untrained mind a need for galvanising the nervous system by actively inciting it with stimuli from without. So far as our present knowledge goes, little seems clearer than that in the acute mental processes there is an inhibition of the highest psychic functions, and that this inhibition in part depends upon an enfeebled state of the neurons which have to do with those functions. If these surmises be correct, it becomes obvious that rest is called for. But whatever hypotheses we may form in respect to these matters, we are justified in saying that from an empirical point of view complete rest produces better results than does any other mode of treatment. The rule that the patient should be rested in

bed is not, any more than it is in cases of excitement, of universal application, and there are some few cases in which the patient seems less agitated when allowed a space within which to roam than when confined to bed, but we would urge that in every case rest in bed should first be tried and should be persevered in unless it is obviously contra-indicated. If it is possible to keep the patient's bed on a verandah or in an open-air shelter it will prove highly advantageous, and in any case he should be supplied with as much fresh air as is possible. The next point of vital importance in the treatment of depressed patients is to remember that no patient should ever be treated otherwise than as possibly suicidal. Ceaseless supervision is imperative, whether the patient be agitated and constantly talking about the necessity of easing himself of the burden of life, or whether the patient is not patently thinking of the matter at all. Every possible method by which the patient can take his own life should be thought of and guarded against. No sharp or pointed instrument should at any time be within reach of the patient. Patients have been known to strangle themselves under the bed-clothes with handkerchiefs, or with pieces of material torn from their clothes, or with string, or with their own hands. Others have hanged themselves from their bed-posts or from gas-brackets, have cut their throats, or have opened veins or arteries with pieces of broken china or glass, or have used the fumes of gas or of stoves to asphyxiate themselves. Medicines, and especially such as are poisonous in large doses, should not be kept in a patient's room or indeed anywhere where he can possibly get at them. Patients deprived of all deadly weapons may for days or weeks lie in wait for an opportunity of throwing themselves from a window or over the bannisters, and the deed has not infrequently been done in the twinkling of an eye, even in the presence of the nurse. It is important, therefore, that windows should be so checked that they will not open sufficiently to admit of the passage of a body, or that they should be guarded in some way by gratings, or that the bedroom should be on the ground floor. When a patient is going up or down stairs, he should be so assisted that he may easily be prevented from throwing himself from an upper to a lower floor. It is sufficient to mention these points in order to emphasise the supreme importance for the utmost vigilance. No patient of this class should ever be left alone for a single second or allowed out of sight in the lavatory, or bathroom or elsewhere.

Hydrotherapeutics have not a very large place in the treatment of depressed states, but it sometimes happens that warm douches, baths and packs are sedative and hypnotic. In cases of bad insomnia, such methods should be tried, and if successful are preferable to hypnotic drugs. The bromides, chloral and other hypnotics already mentioned in the treatment of states of excitement, are also of use in states of depression. There is abroad a not uncommon impression that such drugs, and especially the bromides, are contra-indicated when patients are depressed. This is certainly not so. It is true that in some few cases depression seems to be increased, but these form a very small percentage of the total number in which either no bad effect is seen, or a good effect is produced, and it is in consequence well worth while to use such medicines until in a particular case they are found to be either harmful or useless. We have no means of determining in which case drugs are likely to be useless or harmful, but in the event of agitation being a marked symptom, it is very likely that they will produce a good result. Opium also has its uses, and given at first three times a day in small doses of 5 min. of the tincture, may be rapidly pushed until 30 or more minims are given three or four times a day. The constipating effects of opium must be remembered and counteracted. In all cases where drugs are being administered, their daily effect should be noted and the dose should be varied with the condition of the patient. It sometimes happens that small rather than large doses suit patients and that hypnotics are better given every other night than every night. As the physical condition improves, it will in many cases be found that the mental symptoms abate. When such is the happy result treatment may gradually be relaxed, the relaxation, however, always lagging behind the point at which the patient has arrived. If, however, with physical betterment there is not corresponding mental improvement, provision has to be made for the proper regulation of the patient's life, combined with such occupation and amusement as he is capable of. This may be undertaken either in an institution or in a private house, but we regard the governing factor to be the amount of attention which can be given to the patient. We have no doubt that many patients who appear most hopelessly demented may by a process of re-education be lifted above the level at which they are as a rule left, but the process of re-education is so lengthy and tedious and the results often so meagre, that the work is particularly disheartening and is but seldom undertaken. From a broad standpoint it may be laid down that the question of whether the patient is best in an institution or in private care is decided firstly by the degree of

eccentricity of his conduct and secondly by the amount of skilled care which can be given him. In an institution a patient may be easily lost, so far as treatment is concerned, in the multitude of his fellows, while in private single care it may be impossible to afford him the experienced professional skill, the amount of society and the quality of work and amusements which can be provided in a well-conducted asylum.

States of excitement, of depression and of confusion may occur in maniacal-depressive insanity, in the exhaustion and toxic psychoses, in dementia præcox, in general paralysis, in epilepsy and in alcoholism, and, according to which entity the symptoms appear to be incidental to, treatment may somewhat be modified. Where it seems probable that maniacal-depressive insanity is the substratum of the symptoms, treatment will be as above indicated, but whereas other attacks may almost certainly be expected to occur, the patient should be warned to keep a watch over his weight, his sleep and his appetite, and on the slightest suggestion of a recurrence to report himself to his medical adviser. If, in addition, he lives moderately with regard to work and to amusements and can manage to avoid those emotional stresses and worries which sometimes appear to be the immediate forerunners of exacerbations, we may hope that he will stave off some attacks and abridge those which do occur. In the matter of the exhaustion and toxic psychoses and of alcoholism, it is clear that prophylaxis is all-important. For general paralysis we have at present no specific, and treatment has therefore to be symptomatic. In mental disorder of epileptic origin, treatment is precisely similar to that employed for the more ordinary somatic symptoms. It should be remembered that acute epileptic mental symptoms are of very rapid onset, that excitement and violence may be great and that symptoms rapidly abate. On the first signs of the onset of symptoms, skilled nursing help should at once be requisitioned in order that the patient may be prevented from injuring himself or others, and if it cannot be provided, it is probably desirable at once to send the patient to an asylum. If sufficient help can be employed, it is often feasible to keep the patient at home, since the attacks, though severe, are but short.

Dementia Præcox.—The observations made above in the matter of the education and mode of life of predisposed persons apply with much cogency to cases of dementia præcox, and even when the malady has made itself evident by such pronounced mental symptoms as induce the relations and friends to seek medical advice, much may be done by close attention to somatic and mental hygiene. The more serious symptoms may be abated and even abolished, and the patient may for years live in the world at large a life by no means useless or unpleasant, though of restricted activity.

Psychasthenia.—The symptoms of psychasthenia are notably exacerbated by anything which lowers the standard of somatic health. Fears, especially if about the state of the body, now appear to be justified, and it is argued by the patient that if some gloomy forebodings have become realised there is no reason why others also should not. Psychasthenic persons are probably more prone to nerve exhaustion than are those of normal constitution, and during the period of such exhaustion the peculiar symptoms of psychasthenia will become more marked. Among women symptoms are worse during the catamenial periods and at the menopause. Bearing these various data in mind, therapeutic efforts must obviously be directed towards fending off those circumstances in which it is possible that disease may be contracted. Here, however, another pitfall has to be avoided, for it is to be remembered that the fear of catching disease may replace other fears and prove to be even a worse nuisance. The treatment of the psychasthenic in the enjoyment of good bodily health and living under hygienic conditions is of very great difficulty, and above all, calls for the utmost patience. Unless indicated for some special reason, for instance sleeplessness or constipation, drugs are of no value and reliance has to be placed upon psychotherapy. The methods of psychotherapy are various, some being simple and some complex. Fundamentally this mode of treatment depends upon the operation of one mind on another, and to some extent all medical treatment involves its use. In the simplest cases the mere assurance by the doctor that the illness of the patient is not serious results in immediate amelioration of symptoms, and there can be but little doubt that in an enormous number of such small ailments as are met with in the ordinary run of general practice, the mental ministrations of the doctor are as valuable as his physical medicaments. The physician may, however, go further, and, in addition to endeavouring to get the patient into a frame of mind which is confident of the efficacy of the means employed and hopeful of the outcome, may make use of the methods of suggestion, persuasion and re-education. Unfortunately, these methods are in extensive use amongst charlatans who employ them indiscriminately and as if they were panaceas. It will be found that in most of the "cures" vaunted by laymen of whatever denomination, such good effects as have accrued can be traced to the effect of the

method of administration, which is not uncommonly arresting, and to the amount of faith which has been instilled into the patient by him who has set out to heal him. The subject matter of the "faith" is not seemingly of much importance, and it may take the form either of crass credulity as to the influence of the stars upon human health, or of belief in the power of charms, "bone-setting," patent medicines, bread pills, "electric belts," "rheumatic rings," or "placebos," or of belief in the healing power of holy waters, or of natural springs, or of belief in "mind-cures," "higher thought" cures, Christian science and other similar fashionable nostrums; or, lastly, of an elevated faith which is not wholly satisfied with the purely material interpretation of vital phenomena. Each of these varieties of "faith" has issued in the relief of suffering, but unfortunately the effects are haphazard and are as likely as not to be mis-applied and at times to result in disaster. The efforts made by him who practises psychotherapy as a medical practitioner are directed towards making the treatment as little haphazard as possible, and to applying it in such cases where other modes of treatment are not likely to be attended by better results. Properly to do this means that accurate diagnosis is of the first importance. Where disease is associated with somatic alterations, psychotherapy is of very little use, though it is appropriately employed in putting heart into the patient and in getting him to bear the ills he has with courage and equanimity, for even in organic disease the cheerful stout-hearted patient has a better chance than the querulous and pusillanimous. In functional disease the case is different and psychotherapy is of considerable and perhaps of supreme use. In psychasthenia, suggestion under some degree of hypnosis has occasionally the effect of suppressing particularly obnoxious fears, imperative ideas, or obsessions, but that is, as a rule, the limit of its usefulness. Persuasion and re-education are more radical methods and seek to alter the patient's outlook on life and his mode of regarding its ills. So far as morbid fears are concerned, it is sought to convince the patient of their unreasonableness and the idleness of permitting conduct to be influenced by them, and so far as obsessions are concerned, it is sought gradually to break the patient of the faulty habit by the exercise of his inhibition. These processes take much time, and when ineffective are so because a sufficiency of time cannot be given to them, or because the patient seeks shorter cuts to his cure. Psychasthenics are not infrequently the devotees of the priests and priestesses of various cults, the distinguishing feature of which is their novelty to the patients, while such good as may derived from them is probably in proportion to their capability of withdrawing the attention of the patient from himself and concentrating it upon something more worthy. The last methods of psychotherapy which we need mention are those which are grouped under the title of psycho-analaysis. At the present time we do not believe that it is possible to assert of the newest methods of psycho-analysis anything more definite than that they constitute a very interesting contribution to psychological investigation. Their therapeutic value is unproven, though it is certain that relief of symptoms may occur during the time that they are being practised. To any one who has made use of psycho-analysis it must be plain that the possibilities of mistake are legion, while the results hoped are for not always obtained even after the expenditure of much time. In psycho-analysis an endeavour is made to explore that part of the patient's mental processes of which he is himself unconscious, and there to find a special group which may be regarded as the precursor of the symptoms of which the patient complains. This part of the patient's mental make-up is analysed by such means as the study of time-reactions, of dream states and of unwilled ideational associations. By examinations such as these a trail may be discovered which being further followed may lead to the lair of the occult complex. When it has been discovered and the connection between the symptoms and the complex laid bare, it is expected that the symptoms will abate by a sort of reconciliation between the complex and the rest of the patient's mentality. Such, roughly, are the procedures of psycho-analysis, while the explanation offered is that certain affective processes of an unpleasant nature are put out of consciousness by the sufferer, and, though out of sight and mind, still continue to initiate processes which issue, all unknown to consciousness, in the form of morbid phenomena.

Paranoia.—In paranoia or delusional insanity the prevention of the development of the delusional system is very difficult, if indeed it is at all possible. Persons who are easily ruffled, vain and suspicious, should, if their particular traits of character are recognised sufficiently early, be specially trained so that these bad qualities may be diminished or eradicated. When delusions have so far advanced as to be recognised as such by casual observers, it is generally too late to hope to delay the progress of the malady, and asylum treatment has usually to be advised. In some cases it may be possible, where the delusions only result in mild eccentricities of conduct, for the patient to pursue his ordinary mode of life, but it is unfortunately not infrequently

the case that the patient, considering himself persecuted, seeks to avenge himself upon the supposititious authors of his wrongs, and in so doing he may become a very serious nuisance and indeed may commit savage assaults or homicide. Where the patient's attitude of mind suggests the possibility of such conduct, it is obvious that he should be placed in safe custody, both for his own sake and for that of others.

Moral Imbecility.—As in the case of idiocy, treatment consists in an education adapted to the patient's diminished mental accessibility. Whereas the normal individual is quickly taught to discriminate between good and bad conduct, in the abnormal individual of this class the insistence in education of the differences between good and bad has to last over a longer time and to be more emphatic. Even so very little impression may be made, and in these circumstances the treatment of the patient consists in placing him in such an environment that he cannot have many opportunities for the gratification of his particular vice.

Feeble-mindedness.—The treatment of the feeble-minded lies in the proper care of their bodies and the putting to the best possible use such mental faculties as they may possess. The educability of idiots, imbeciles and weak-minded persons varies enormously. In the lowest grade it is difficult to teach the children even to sit up, while the control of the sphincters, standing and walking, are never learnt even after the expenditure of much attention and time. In the next higher grade, walking and some sort of control of the sphincters may be taught, but the child does not learn to talk or to use his hands to any purpose. A little higher up the scale the child may be able to enunciate a few simple ideas and to use his hands for such actions as spooning food into his own mouth, turning the handle of a barrel organ, or toying with a ball. Yet higher up in the scale of educability of the feeble-minded child powers of helping himself to food and drink, of dressing and undressing, of playing uncomplicated games and of learning such handicrafts as basket-making, shoe-making and laundry work may be acquired. The treatment of the feeble-minded depends, then, upon their educability, while the degree of that educability can only be determined by experimentation in every individual case. Directly a child is recognised as feeble-minded its special education should be commenced, and no delay should be allowed on the ground that the child "may grow out of it." It must be remembered that to get the most out of an educational system it is desirable even in the healthy child that his physical health should be good. In the case of the feeble-minded, we find a class who are weakly and prone to the infections and to early death, so that more than ordinary care should be bestowed upon hygiene. It is not necessary here to go into detail, and it must suffice to insist that all those measures which in a normal child are desirable are, in the case of the feeble-minded child, imperative and indeed vital. The education of the child is obviously best undertaken by those who are specially trained for the work. Among those who are not well off, it is advisable that the child should be removed to an institution. Mothers, though as a rule extremely devoted to their unfortunate offspring, are not the best educators, nor amidst the demands of their domestic duties can they give that amount of attention which the defective child demands. The first matter of real importance is to endeavour to educate the centres controlling the bladder and rectum, or, if it prove impossible to instil control, to get the centres to act automatically at regular intervals. This can in many cases be brought about after months or years by placing the child upon the close-stool at regular intervals and leaving him there until a result has been obtained. Some children are fortunately rapid in the acquisition of control over the sphincters, while others never learn and during all their lives are wet and dirty. The next important feature in education is to induce in the child a sense of position and a rudimentary knowledge of the feeling of various objects. He may, for instance, be fastened into a swing with his feet stuck out straight in front of him. The swing is then set in motion and at the end of its excursion a cushion is so arranged that the feet of the child come in contact with it. After a time the child is made to feel his feet by standing upon them and ultimately to perform those movements which result in walking. The education of the defective child differs from that of the normal child in that there is in him a lack of spontaneity and power of attention. The normal child, having found his feet, very soon of his own initiative moves his legs, but the defective child of low grade does not, and spontaneity has to be replaced by the laborious efforts of the educator. Similarly with the movements of the hands and of those muscles connected with speech. In the case of the attention the normal child, if sufficiently interested, can be got to attend to that which he is looking at or listening to, or trying to do. The abnormal child, on the other hand, cannot, perhaps, be got to attend at all, or at most for insufficient periods of time, and it is only by patiently directing upon him stimuli of an elementary variety that at last some sort of impression is made. Step by step the extension, shape, hardness and softness, weight and

temperature, of various objects have to be inculcated, the teacher remembering that whereas in a normal child a single experience may suffice to indicate a difference, say of temperature, between one thing and another, in the abnormal child a very much larger number of experiences lasting over a very much longer time is necessary. In the matter of speech movements of the mouth may have to be taught before the movements can be co-ordinated for the purpose of enunciation. If speech has been acquired an attempt should be made to teach the child to read, write and draw, while at the same time the use of certain tools, requiring no great dexterity, should be practised. It is impossible here to enter into a description of the technique of the education of the feeble-minded, and only the broad outlines can be indicated, but it should be remembered that it is most important in carrying on an educational programme not to forget the child's moral character. In most cases a rudimentary sense of right and wrong can be evolved by an appropriate scheme of mild rewards and punishments. The infliction of physical pain is not only wholly unnecessary, but is harmful in that it produces a distrust of just those persons upon whom the child should implicitly rely. Punishment should consist in the deprivation of those small sources of satisfaction which are known to please, while, on the other hand, good conduct should be rewarded by a marked display of approbation on the part of the teacher and perhaps by the bestowal of some simple reward. In the education of the feeble-minded, the personality of the teachers and attendants is of supreme importance. The good teacher who is persistent, patient and sympathetic, can produce results which are sometimes astonishing, while the pupils of the teacher lacking these qualities will in all probability show but little or no progress.

Epochal Insanities.—Certain periods of life are, among predisposed persons, those at which there is a peculiar liability to mental disorder, and it has therefore been customary to describe such disorders occurring at such periods as "Epochal Insanities." They are, however, for the most part, better classified under other headings, it being noted that the liability to suffer from them is greater at certain ages than at others. Taking such epochs in chronological order, we may first consider abnormal states occurring at the time of puberty. Both somatically and mentally, considerable changes accompany the commencement of sexual life. The forces which come into being within the individual, and which blindly seek expression, chiefly indicate their presence, so far as the mentality of the person is concerned, by an exaggerated self-consciousness and introspection. In the normal individual such exaggerations sooner or later subside, but in the abnormal are intensified and last over a considerable time. It is imperative in the treatment of such patients that they should live as healthily as possible. Out-door life, with plenty of sleep and good food and an avoidance of fatigue either mental or bodily, are the chief means that should be employed. On the psychic side the influence of a sound guide and friend is of supreme importance. Some patients of this type have no notion of the meaning of the emotional disturbance within them, and from the physician's point of view we see no particular reason why they should be enlightened; others have a very full knowledge of sexual matters and may seek to gratify their appetites by natural means, by homosexual relations or by masturbation. With such it is best to be perfectly frank and in plain terms to set forth why such practices are reprehensible from physical and moral points of view. Symptoms are not, however, always limited to mere exaggerations of ordinary mental states, and it occasionally happens that during puberty or the years immediately succeeding it, *Dementia Præcox* begins to develop. This syndrome is held by some to be significant of the "shut-in" or ultra-introspective personality, and whether this be so or not, it is as well to bear in mind that the most prominent early symptom of dementia præcox is the diminution of affectivity and the consequent loss of interest in persons and things. The earliest symptoms of dementia præcox are not always distinguishable from mental states which do not pass subsequently into the developed disease, and as a result the treatment of these earliest symptoms is the treatment of such exaggerated normal mental states as have been referred to above. At a later stage of the disease treatment is as suggested in the paragraph upon Dementia Præcox.

The insanities associated with the climacteric have been termed epochal, but for the most part they are more justly classified among the *Exhaustion Psychoses* and treated accordingly. In the case of women the process of involution may be regarded as dating from the climacteric, and mental affections starting at or after this epoch may be classified, in the absence of the causes of exhaustion, as involutional. Here again, from the therapeutic point of view, the change in nomenclature is not very illuminating. Those predisposed by heredity or previous attacks to mental affections should be particularly careful at the climacteric to husband their physical forces, and the chief points to which the physician has to pay attention are the enforcement of the rules of an appropriate

régime in which food is plentiful and rest is taken in proper quantity at the proper time. It may further be necessary to treat an excessive loss of blood by such drugs as calcium lactate, ergot, styptol, lodal and iron.

Among the epochal insanities are included the disorders of senility. Among women the termination of one of the most important functions of life takes place, in most cases, punctually within a given lustrum, and the commencement of involution may definitely be dated from that period. Among man there is no such comparable abrupt cessation of function and involution is of more gradual onset. In both sexes senility may be premature or may be delayed, and its appearance is gauged by physical and mental characteristics which are so well known that it is entirely unnecessary to enumerate them here. In addition to the normal accompaniments of age there may appear abnormal somatic and mental phenomena, the latter including states of confusion, of excitement, of depression and of dementia often associated with hallucinations. Treatment must in part be ameliorative and in part preventive. In states of confusion, excitement and depression, treatment must be as above laid down, while prophylaxis lies in contraction of the patient's field of activity, whether digestive, vascular, respiratory, renal or nervous. The progressive dementia of old age requires an increasing amount of nursing attention, until eventually the old patient stands in need of as much looking after as a newborn infant. Among the most distressing symptoms, though fortunately of not common occurrence, is that of libidinous conduct. One of hitherto irreproachable repute may in his old age take to the commission of such indecent acts as may bring him into the hands of the police. It is seldom that such symptoms are not in association with some degree of dementia, but it is quite obvious that in any case, for the sake of the community and of the individual, close and constant watching by a nurse or attendant is indicated. Symptoms of this character are sometimes ascribed with a certain amount of justice to prostatic troubles, and it is at least as well to inquire closely into the condition of the bladder. Other sources of peripheral irritation, for example eczema or pruritus, should be looked for and remedied.

Puerperal Insanities.—As in the case of the epochal insanities, so in the puerperal the incidence is chiefly upon those women who are predisposed to mental disorder. Certain exciting factors have a special incidence during pregnancy, childbirth and the period of lactation, and the most important are those tending to produce exhaustion. The sickness of pregnancy may, for instance, so interfere with the patient's nutrition that her nervous system becomes entirely exhausted and the symptoms of an exhaustion psychosis may follow. Similarly with albuminuria or salivation or any other somatic disorder which may occur during pregnancy. Worry of any sort, whether it be in connection with the circumstances of conception, with the family or with business, has also a wearing and exhausting effect. The normal excitement and physical stress of parturition, if at all exaggerated, may readily eventuate in mental symptoms, while during lactation the patient may become worn out by suckling her child when she is physically unfit for the work. Indeed, it must constantly be remembered that any physical or mental work entailing fatigue may put the pregnant, parturient or nursing mother in danger. Other causes producing like symptoms are the infections, and there is obviously a special liability to septic infection at childbirth. These various etiological factors are here mentioned because treatment should for the most part consist in particularly cautious prophylaxis in the case of predisposed persons. In one of known neurotic disposition or having a bad family history, or in poor physical health, exhausting occupations should be given up and any such physical disorder as may be present vigorously treated; while for this, if for no other reason, antiseptic precautions should be practised at childbirth. If prophylaxis unfortunately fails and symptoms develop, treatment will be as above indicated under the heading of the Toxic and Exhaustion Psychoses. There are, however, certain women who in the absence of any of the above-mentioned causes of mental disorder break down before, at or after childbirth. It may not be possible to attribute their symptoms to exhaustion or to any concomitant physical disorder, and perhaps the only apparent causative agency lies in a faulty personal or family neurotic history. Such persons can seldom pass through life without in some way giving way under stresses which would leave a normal individual untouched. There is no doubt that child-bearing and rearing involve very considerable exertions on the part of the female and expose her to numerous dangers, and with this in mind it is often a moot point whether the risks of pregnancy should be incurred. The problem as to whether pregnancy when it has occurred in such persons should be artificially terminated is an especially difficult one and there is certainly no golden rule which applies in all cases. It may be remembered that pregnant women who show signs of mental disorder in the early months of pregnancy often rapidly recover as pregnancy advances, and that therefore unless the symptoms are very grave it is better not to interfere. If, however,

nutrition is very seriously jeopardised, as for instance in uncontrollable vomiting, both the vomiting and the mental symptoms may be relieved by abortion. If mental symptoms show signs of occurring during the period of suckling the child should at once be weaned.

M. C.
E. D. M.

GENERAL SURGICAL TREATMENT

PREPARATION FOR ANÆSTHESIA

Of all precautions most necessary before an operation under surgical anæsthesia, perhaps the one most frequently omitted is that of rest. No matter whether the patient is robust or not, rest in bed for thirty-six hours beforehand should be taken, and in the case of weakly and debilitated subjects, especially when the operation is not a trivial one, this should be proportionately increased. The diet should be nutritious and easily digestible, and alcoholic stimulants usually omitted. If the operation hour be early a light meal, such as clear soup and fish, may be taken the previous evening. In the morning, if time allow, there is no objection to a cup of tea and a small piece of dry toast being taken two and a half hours previously. If the operation be fixed for mid-day, a small light breakfast of fish may be permitted so long as about four and a half hours are left for digestion. Clear soup should be given two hours previously if the operation takes place in the early afternoon. In weakly subjects before serious operations, enemata, of beef tea, coffee, 5 per cent. dextrose in water, etc., may be given an hour or two immediately beforehand.

It must be remembered that although it is dangerous to anæsthetise a patient when there is undigested food in the stomach, it is probably more so to give an anæsthetic, especially chloroform, to a patient who has undergone too long starvation. This is especially so in the case of children and weakly adults, and in the presence of sepsis.

In regard to the bowels, it is desirable that they should be well opened the previous day. An aperient may be given thirty-six hours before, and if necessary an enema the evening before. A good night's rest should be ensured, and a hypnotic, such as bromide or heroin, when natural sleep is improbable. Mental quiet as well as bodily rest is very desirable before an operation, and the conversation and excessive sympathy of relatives and friends should be eliminated or minimised.

The administration of morphia, hyoscine, etc., immediately before an operation is not desirable as a routine, but should be reserved for neurotic and nervous subjects and given about one hour beforehand. As an aid to relaxation for operations in the upper zone of the abdomen, they are, however, useful, and diminish the amount of anæsthetic required.

The avoidance of cold and loss of heat during an operation is most essential, and not only should the operating-room be quite warm (70–75° F.) but the patient's chest especially protected by light warm clothing or gamgee tissue. For children, a gamgee jacket is very useful for this purpose. The patient should always be anæsthetised upon the operating table when possible, the movement from a bed or another room during anæsthesia being dangerous for the patient, and rendering it extremely difficult for an even and quiet anæsthesia to be maintained afterwards. It also renders post-anæsthetic vomiting more probable.

Finally, strict silence should be maintained in the room during the induction period and any disturbance of the patient forbidden until anæsthesia is established.

Treatment of Post-Anæsthetic Complications

Although the after-treatment of the patient rests entirely with the surgeon, the anæsthetist is not infrequently consulted when complications arise. Vomiting, as a rule, after a properly administered anæsthetic is transient and almost negligible. Occasionally it persists for twenty four hours or more and may be very difficult to stop. Frequently a copious draught (half a pint) of warm water rendered alkaline with sodium bicarbonate will by acting as a gastric douche give much relief after its return. It may be repeated at half-hour intervals two or three times if necessary.

Aspirin and potassium bromide (20 gr. of each), given in saline per rectum, is sometimes very successful.

Heroin ($\frac{1}{6}$ gr.) hypodermically is also beneficial, much more so than morphia, which in some people undoubtedly produces sickness.

Delayed anæsthetic poisoning, particularly after chloroform, is occasionally met with. The vomiting is severe and persistent, coming on after twenty-four hours or later. There is an odour of acetone about the patient, and acetone may be detected in the urine. Other symptoms are jaundice, restlessness, delirium, periods of screaming alternating with apathy, and a rapid pulse. In a well-marked case death may occur in two or three days. Unfortunately the treatment is very unsatisfactory. Sodium bicarbonate

(1 dr. to 1 pint) solution should be given by the mouth, in a copious draught as a gastric douche to begin with, and then in smaller quantities every quarter of an hour. The solution should also be given continuously per rectum with the addition of 5 per cent. of dextrose.

Hæmatemesis occasionally occurs after an operation. It is doubtful whether it can be attributed to the anæsthetic, and probably has its origin in some infection of microbic origin of the gastric mucosa. Cases have occurred after the Trendelenburg position has been adopted, especially in fat and plethoric subjects.

It hardly ever persists. The avoidance of any fluid by the mouth is the only precaution required. C. H.

THE CARE OF SURGICAL CASES

This subject may be considered under the following headings—

1. General.
   (*a*) Preparation for operation.
   (*b*) Care of the patient during and immediately after operation.
   (*c*) General treatment after operation.
2 Special.
   After-treatment of special cases.

1. *A*. Preparation for Operation

The Patient.—Speaking generally, there should be as little interference as possible with either diet or method of life before an operation. To this rule, however, there are many exceptions; thin, anxious, overworked women will benefit greatly by an enforced rest before an operation; on the other hand, the plethoric, bovine butcher, who has never known a day's illness and has lived hard all his time, may give rise to most serious trouble if he is run *secundum artem* into a nursing-home and operated upon immediately. Such a type may well be put to bed and given a moderately light diet for some days before operation, absolute rest being insisted on. Another type—the person who has led a tempestuous and immoderate life—has to be considered. The practice of stopping all alcohol in a case of this kind cannot be too strongly condemned, and may lead to the direst disaster. On the other hand, a few days' partial rest in bed with moderation in alcohol and aperient treatment will be of very great benefit to such a patient. A rest in bed for a week or more is the best possible preparation for a healthy muscular individual before an abdominal operation if there is the slightest doubt in the case. The patient should have an aperient at least thirty-six hours before operation, and a simple enema of soap and water should be given two hours before the operation, followed, if necessary, by one immediately before the operation. The aperient is only too commonly delayed until the night before the operation, and then either the bowels are not properly relieved or else the patient has passed a bad, restless night, or both. This can hardly be considered a good preparation for a trying ordeal. The patient, therefore, should, after the aperient, spend the day before the operation in quiet rest either on a sofa or in bed. It is customary to advise that the patient should have no food of any kind, liquid or solid, for three hours before the operation. It is very doubtful whether this is wise. From personal experience, I firmly believe that, more especially in children, the period of starvation should not in any circumstances be more than three hours, and it is my usual custom to order about two ounces of stimulating fluid like Bovril or clear beef-tea two hours before the operation. Most anæsthetists will now agree with this opinion and believe that in cases where there has been over-starvation there is often, especially in young adults, continued vomiting and heaving processes which add not a little to the surgeon's vocal repertory.

The part to be operated on should be shaved the night before operation; eight hours before the operation it should be painted with $2\frac{1}{2}$ per cent. iodine in rectified spirit; the skin should be painted over a considerable distance outside the area of operation and the iodine should be allowed to dry on. This should be repeated just before the patient is brought into the operating theatre. This method of preparation of the skin is quite effective, and as compared with the old method does not interfere in any way with the patient's comfort.

General.—The surgeon should be asked by the practitioner if he desires any special preparations to be made. Usually the first question to be settled is whether the patient should be operated on in a nursing-home or his own home. If his home is quiet, without a superfluity of children or other livestock, there is no doubt that it is much better for the patient. It may give the practitioner and surgeon more trouble, but the comfort and saving of expense to the patient should entirely overweigh such considerations. Any reasonably clean room can easily be made into an admirable room for a surgical operation without great trouble or disturbance to the rest of the house. Moreover, it is not unreasonable to assume that fewer noxious germs will lurk in the quiet precincts of a home than in a nursing-home where there is a continual coming and going of dirty boots, not to mention the number of septic cases which have to be operated on in such

places. Moreover, the effect to the patient of lying up in home surroundings is usually infinitely better. Of course, in such cases, the actual surroundings and psychical state of each individual patient demand close study.

If it has been decided that the patient shall be operated on at home two competent nurses will probably be required. In the case of a minor operation one nurse may prepare the room and depart once the patient is out of the anæsthetic. The question of the competency of the nursing is again one which should largely influence the practitioner in settling where the patient is to be operated on. If the patient is sent into a nursing-home, no choice of nurses can be made. On the other hand, a careful choice can be made if the nurse is brought to a private house. The necessary qualifications for a good surgical nurse are many. Despite popular belief, most nurses have a habit of talking too much, and, however keen may be their surgical enthusiasm, the patient, whether male or female, will usually not have the profoundest interest in the details of his or her own operation; nor will he listen with breathless delight about the laying out of a corpse in the next room; nor is it to be anticipated that such an account will materially alter his condition for the better. The nurse must be absolutely reliable and truthful. With modern surgical technique but little is required of her, and that little must be most carefully and accurately carried out, for on her capable and self-reliant account of the condition much may depend. A very highly trained gold-medallist once reported to me that her patient was very cross and cantankerous and restless when, as a matter of fact, he was very nearly dead with internal bleeding after an operation for hæmorrhoids.

Local Preparation.—The room where the patient will be nursed should be of fair size (14 by 10 by 10 feet is quite large enough), well ventilated and without side-doors to other rooms. Blocks a foot high, which can be made by any carpenter, should be in readiness for raising the bed in all cases. The bed should not be a family one capable of holding six. It should be a light iron bedstead, not sagged in the middle, and so placed that the nurse can get on either side of the patient. We have found that known as the "Taunton" bedstead in hospital use to be an admirable one. If there is sagging of the frame a board should be put across it.

If the patient is likely to be in a dangerous state after the operation, it is well to consider the question of a water-bed from the very first. On the other hand, it is to be remembered that some patients cannot stand a water-bed, and moving about on a water-bed induces in them a sort of "sea-sickness." Such small points as seeing that the windows open and shut without noise, as also the door, are of real benefit to the patient. Again, a loose, creaking board in a floor can easily be remedied in three minutes before the patient is brought into the room, but will drive him nearly crazy if left to his days of convalescence.

The nurse will require in the room the following—a rectal tube, female catheter or soft rubber male catheter, an enema fountain syringe, bed-pan (the flat pattern should be used) and bed-urinal, towels, basins, feeding-glass, a feeding-tube, clinical thermometer, ordinary thermometer and charts. A word of warning may be given to her with regard to the thermometer. The temperature of the room is not to be obtained by putting the thermometer into the fire or in the fender or outside the window. The place for the thermometer, again, is not as a sort of ikon four feet above the head of the bed over the patient, but should be placed about the middle of the frame of the bed where it can readily be seen by the doctor without the patient observing it. Speaking generally, the temperature of the room should be 65° F. at this part. The nurse can usually be relied upon to keep the temperature, pulse and charts, but there is an absolute fetish amongst many at once to remove and destroy all excreta; despite the enormous importance in many cases of their being kept for the practitioner's observation. In a surgical case, for the first three days, the practitioner will do well to insist at the very beginning that no excreta are thrown away without his express permission. The inevitable bottle of brandy can really be quite well left in the dining-room. The room should not be allowed to present the appearance of a horticultural show or a hearse in summer; a presentation of an electric fan or ice-bags will delight the patient more than a wilderness of flowers.

The Operating-room.—This, if possible, should face north and have a good light. Its choice will often be decided by the presence or absence of electric light. A good light is essential, and it is usually more satisfactory to fix up a powerful electric light for the occasion. All hangings, pictures and carpets should be removed, if possible thirty-six hours before the operation. The walls should then be rubbed down with a damp cloth which is frequently rung out with boiling water. The linoleum should be left. The floor is now scrubbed in the usual way and rinsed with 1 in 20 carbolic lotion. Meanwhile the window is open and a thorough draught maintained so as to get the dust out of the room. The room is now sterile and should be respected as such by the nurse. Thus the family are not invited at this stage to inspect the proceedings and the nurse will do well to put

on white canvas tennis shoes, which have been previously boiled, when she is walking in the room. The modern shoe should be commented upon severely and with decision by the practitioner. As the present author only too well knows, it is an imperfect preventative for the entrance of broken glass.

Furniture of the Operating-room.—In most large towns in these days, both tables, basins and operating tables can be easily hired and brought in, usually accompanied by much septic contaminations from the boots of the carter. The present article only deals with what is necessary. Four small tables are scrubbed and polished; if already polished they should be rubbed with turpentine. An operating table long enough to make the patient comfortable; at a pinch a kitchen table thoroughly cleansed will make an excellent substitute, and the "Trendelenburg" position may be obtained by putting one end of the table on two chairs, from which, it may be observed, it will usually slip.

Utensils.—Six enamelled bowls (1 gallon) or wash-hand basins; six enamelled jugs (2 gallons); six enamelled trays (15 by 12 in.). All these should be boiled, rinsed out with 1 in 40 carbolic, and placed, before the operation, on the towel-covered tables. In the preparation of all sterilised towels and utensils it is most important that the hands should be washed in running water, and if possible they should touch nothing not sterile. One cannot labour this point too much.

Dressings.—Now-a-days the surgeon usually brings his dressings in a sterilised box or drum. It is right that this should be done, because it has to be remembered that the ordinary so-called "high-pressure" steriliser cannot be relied on. No sterilisation can be considered to be complete unless the dressings have been sterilised at 260° F. and dried in a vacuum of 20° F., and no painstaking surgeon will be content without having his dressings tested from time to time at a surprise bacteriological party. Some are in the habit of putting in a tube of benzoic acid which changes to a dull red colour after the heat has been at 260° F. for a quarter of an hour. The practitioner desiring further information cannot do better than request an interview with the courteous manager of Messrs. Bell and Croyden, Mr. Marshall.

The surgeon should alone be responsible for the dressings; it is unfair, if the wound becomes septic, to blame the preparation of dressings over which he has no control. At the same time, the nurse should prepare the following "rough" dressings: twelve towels sterilised in a potato- or fish-steamer for three-quarters of an hour. In this way they are not sopping wet and do not require so much handling as when they are boiled. These will be covered over by the dry sterilised towels usually brought by the surgeon, and should be spread out before the operation over the tables which are likely to be used by the surgeon or his assistant.

The prepared dressings brought by the operator usually consist of—

3 dozen sponges, round or flat.
6 large flat abdominal gauze pads.
1 lb. wool.
6 gauze strips, 1 in. and 2 in. wide.
6 surgical towels.
Bandages.
Many-tail bandage.
Safety-pins.

The careful nurse, however, will do well to supply safety-pins herself, as they are often forgotten; moreover, she will stick the ends into a little cake of soap and, in this way, they will go readily through the dressings, and avoid the surgeon's fingers. I would plead strongly in making choice of dressings that two long rolls, one 12 yards and the other 6 of sterilised gauze 5 inches wide be included. The shorter of these two rolls should be put over the spectacle frames which are now largely used as masks by the surgeon and his assistant and which were originally invented (I believe) by Mr. Thorburn of Manchester. The long roll is of great assistance in an abdominal operation. Nothing else except a swab for sponging up blood should be put into the abdominal cavity. Loops of the original long roll can be used to pack round the viscera, etc., and, at the end of the operation, there can be no shadow of doubt if this is regularly used that anything has been left behind.

Lotions.—Most surgeons now use their swabs and dressings dry, and lotions are only used to rinse the hands. The nurse should be ready with these in order to suit the peculiarities of the surgeon. Of these the following are used: (1) normal saline solution, salt 1 teaspoonful to a pint of sterilised water; (2) mercuric chloride 1 in 500; (3) 1–500 solution of mercuric biniodide with methylated spirits to which 25 per cent. of water has been added; and, last and least, (4) carbolic acid 1 in 20.

There should be two thermometers in every operating-room; one close to the operating table to give the temperature of the room; this should register, unless otherwise required, 65° F. The other—an all-glass bath thermometer—should, metaphorically, be up the nurse's sleeve. If a lotion *is* required, she should test its temperature. Surgeons naturally dislike being given either pure carbolic or boiling water when they have asked for lotion to wash their hands, though nurses fail to

realise this. The proper temperature for lotions is 104° F., unless specially directed.

Table.—Every attempt should be made to make the patient comfortable on the table. A little solicitude on the part of the nurse when the patient is getting on to the table, as to pillows for the head, and abstaining from taking off his clothes until he is unconscious, makes a world of difference to the patient's comfort. The table should be covered, if the operation is very long, with a narrow hair mattress. It should be provided with hot-water bottles which should be kept away from the bare skin, and these should be invariably watched by the practitioner or nurse whenever the position of the patient is changed to make sure that they are not being brought into contact with the skin. Remember that burns dry up all human pity and gratitude, and that the nurse's pocket is usually short and that, next to her, the surgeon and practitioner are legally responsible. The usual excuse that neither the table nor the bottles were hot is all nonsense.

A large steriliser or fish-kettle with boiling water *with no soda added to it* should in all cases be ready when the surgeon arrives. The surgeon may want to boil his gloves in it, and, if so, the nurse will not have his thanks if she puts soda in the water. On arrival he will put his instruments in it and attend to other details in the operating-room. The instruments should be boiled for fifteen minutes, so that the patient should be ready to begin the anæsthetic five minutes after the instruments have been put into boiling water. The surgeon and assistants should wash their hands in a room adjoining the operating-room, not in the operating-room, and the less open fire there is in the operating-room the better for the air, since if chloroform is given in a small room, a naked flame sometimes produces chlorine gas.

Counsel of perfection would be that the entire party should enter the operating-room in clean canvas shoes—yet although this is now done in most hospitals, and in some the patient is actually clad in sterilised clothes, it is rare to see any arrangements of the kind in a nursing-home. Now the dressings are opened, and the practitioner and nurse had better leave it to the surgeon. Many use the top of the sterilising box turned over to put some of the instruments on.

All is now ready for the operation to begin, and here I must confess that I think too little account is taken of the psychical condition of the patient. In some few cases of a child or a woman it is thought of, whereas, as a matter of fact, a man is far more nervous before undergoing an operation, and though he conceals his feelings they are nevertheless present in an acute state and are bound to have some effect on his recovery.

I cannot agree with those anæsthetists who insist upon the patient mounting the scaffold in all cases. It is a task of some magnitude to attempt to hoist an unconscious lady of eighteen stone on to an operating table, but, on the other hand, if a trolley or stretcher is provided on the patient's bed, a patient can usually be put under an anæsthetic there, and this is surely the kinder method. It has to be done in the case of a patient who is too ill to walk into the operating-room, and therefore I fail to appreciate why it should not be done in other cases. Much is heard of homes for cats, cruelty to animals and traffic in worn-out horses now-a-days, but little of the topic I have mentioned. If the patient has to come conscious into the operating-room the fewer people who are in the room the better. Moreover, turned-up sleeves and surgical robes are not reassuring. We must remember that the whole mental state of the patient is changed even before anæsthetisation begins. Eternal leave-takings, holding of hands and general endearments are not to be allowed. One other duty of the nurse and practitioner is towards the friends who are waiting. If possible, it is a great deal better to get them out of the house, by force if necessary, but, if they will wait, it will repay the nurse and practitioner if arrangements are made to tell them how things are going from time to time during the operation.

B. Care during and immediately after the Operation

Position of the Patient

1. *The Dorsal Position* is usually used for the operation itself, but it is a bad position for the patient to remain in. If the patient lies on a hard table, backache is very common and continued pressure causes sores over prominent bony points. For the same reason, patients in the dorsal position are liable to bed-sores and are most difficult to nurse, especially old people in whom there is a tendency to accumulation of mucus in the lungs, and as a result hypostatic congestion.

2. *The Prone Position* is used for operations on the back. A pillow is placed beneath each of the patient's shoulders and the head turned towards one side near the edge of the table.

3. *The Semi-Recumbent Position.*—This is the best all-round position for patients of all ages after an operation (except in rectal cases). It is wise to keep all acute abdominal cases in this position until all danger of spreading infection to the upper portion of the peritoneal cavity is at an end. The patient should be raised to about 45 to 60 degrees from the horizontal, the feet braced against a board; to effect this the head of the bed is raised or the patient is raised on pillows. The difficulty in nursing is to

prevent the patient gradually dropping down in the bed, and this is a very real difficulty in heavy patients. An admirable way to avoid this is to have the legs bent and a small padded board about 10 inches high and nearly as broad as the bed well padded on either side placed under the thighs; in order to avoid any uncomfortable pressure pillows or any extra padding can be placed over this and shifted as desired. The board is kept in position by a bandage or straps carried through holes at either end and fixed to the head of the bed. It can be rapidly made. If such a board is not to hand, the patient can be temporarily supported by a pillow wrapped in a sheet and placed under the thighs.

4. *The "Trendelenburg" Position* must be mentioned; this is probably the safest for the patient from the anæsthetist's point of view during the operation, and the patient is remarkably free from severe shock after the operation when this position has been maintained; it is, moreover, essential in most pelvic operations.

It may be noted that the practitioner, unless operating himself, is not legally responsible for the control of the patient during the operation.

With regard to burns, it is important to remember that no hot operating table or hot-water bottles should be in direct contact with the patient, and each time the patient is moved the surgeon should be reassured as to the patient's safety in this respect.

Mere pressure over a hard surface will cause a sore place if the patient has lain in the same position long if the part receiving pressure is not protected by fat, as for instance, the buttock or calves. It is also important to see that the heel is supported for the same reason.

Shock.—It is no part of the present article to attempt to deal with the pathology of shock. The treatment may be taken as follows—

1. *Preventive.*—There should be no prolonged period of starvation before the operation; morphia ($\frac{1}{4}$ gr.) and atropin ($\frac{1}{100}$ gr.) should be given hypodermically half-an-hour before the operation. During the operation the "Trendelenburg" position should be used if possible; unnecessary delay should be avoided in the operation and as light as possible a degree of anæsthesia should be kept up. Above all, there should be no pulling or dragging at the intestines or stomach, and no unnecessary exposure of the viscera. The patient is kept as warm as possible and, if the viscera are exposed or there be a very large extensive wound, as in breast cases, the wound is covered with towels rung out in hot sterilised saline solution. At the same time, it is to be remembered that if these towels are allowed to get cold they are worse than useless.

2. *After the Operation.*—Bandaging the extremities; warmth; brandy per rectum; raising the foot of the bed if necessary; digitalin and strychnine are often recommended hypodermically, but it is probable that neither of these have any effect. Continuous fluid by the rectum provides the best gradual method of combating shock. (Further details are to be found in *The Treatment of Acute Peritonitis.*) Pituitary extract, there is no doubt, has a powerful effect in combating shock. It is, at any rate, more lasting than that of adrenalin.

Infusion of fluids into the tissues. In grave cases of shock two pints of fluid may be injected by a large saline syringe with a needle into the loose tissues such as the axilla. This may be saline solution, *i. e.* salt one teaspoonful to the pint; to this an ounce of brandy may be added and 10 min. of a solution of 1 in 1000 adrenalin. The temperature of the solution, if it is in a jug, should be 103° F., as it cools rapidly. It is to be observed that if the circulation is at all adequate this will be rapidly absorbed. The method of injecting fluid direct into a vein is now considered by many to be absolutely dangerous, as it produces too rapid a change in the circulation and may be the cause of sudden heart failure. The old method of transfusing blood from one patient to another is now obsolete. It is well to remember that nothing can be gained by rapid injection of fluid into the tissues if there is no absorption. Caffeine and sodium benzoate 3 to 6 grains to the pint have also been used as an injection into the tissues, also glucose 5 per cent. Recently, American surgeons have used a mixture of 1 pint champagne to 2 pints of sterilised solution for injections into the tissues, and they speak highly of the extraordinarily stimulating effect of such a mixture. In giving fluid continuously into the rectum it is necessary to remember the following points: (1) In most cases the rectum should have been cleared out first by an enema. (2) A small rubber catheter should be used, and should be inserted quite six inches into the bowel. (3) The fluid to be administered should be kept in a Thermos flask at about 100–103° F., and this should not be raised more than 6 to 8 inches above the bowel. (4) The fluid to be used can hardly be allowed to run too slowly into the bowel. It should be allowed to run at the rate of about half-a-pint per hour. It is controlled by a drop-valve which allows the rate of the fluid dropping through to be seen. (5) Very nearly 50 per cent. of children and 20 per cent. adults will not retain fluid by rectum despite all the care of the administrator.

C. General Treatment after Operation

Treatment of the Wound.—The details of treatment of the wound belong more strictly to the surgeon. An aseptic wound is now gener-

ally painted with iodine in rectified spirit; we are personally in the habit of painting it, however, with Friars' Balsam made with ether instead of alcohol. This sets rapidly and excludes the air from the wound and is entirely unirritating and aids healing. A little wool is placed over this, and the whole can be loosened rapidly by acetone and the stitches removed on the eighth and tenth day. Drainage tubes are not often used at present; when they are, they should be removed with every possible precaution of surgical cleanliness between the twenty-fourth and thirty-sixth hour after the operation as the surgeon desires. The wound if closed is not examined unless there is good reason to believe that some septic process has set in. This is evinced by (1) pain; (2) continued rise in temperature and pulse-rate. In this connection, it should be remembered that an early and sudden rise in temperature means nothing. It is a very frequent occurrence, with children especially, after operations where there has been some extravasation of blood into the tissues. In such cases, a rise of temperature in the morning, dropping in the evening, is the rule. This "traumatic" temperature, as we may call it, usually occurs within the first twenty-four hours; sometimes within forty-eight hours after operation.

Dressing of Septic Wounds.—If the wound has become septic, stitches should be cut and removed eight hours after cutting, for the pulling out of a tight stitch in an inflamed area is exquisitely painful, and fomentations should be afterwards applied. As a rule, such treatment is much preferable to putting on gauze. Pain is decreased and the wound is rapidly closed. At the same time, a purge is given; perchloride of iron can be given in a draught, and there is little doubt that it is well to examine the wound bacteriologically with a view to obtaining an autogenous vaccine for subsequent use. The fomentations usually used are boracic, carbolic or aluminium chloride. In other cases, continuous baths of binioide of mercury or hot boracic lotion can be used. I am firmly convinced of the great advantage to be obtained from the use of an iodine preparation now known under the name of "Iodex." It appears to be quite unirritating in septic wounds and they clear up rapidly when it is rubbed into them. I am now in the habit of constantly employing it in all septic cases.

Thirst after Operations.—The probable cause of the thirst which is so common after operations is the loss of fluid to the body by the purgation before operation, increased mucous secretion, vomiting or hæmorrhage. In addition, the secretion from the mucous membranes is inhibited.

In the treatment of thirst, the first indication is to give plenty of fluid even if the patient has vomited. Iced water does not appear to remove it. Hot weak tea is often the best or lemon juice prepared by mixing together the juice of one lemon, one ounce of glycerine and a pint of water. Washing the mouth out with equal parts of glycerine and rose-water often gives very considerable relief. On the whole, however, the best remedy for severe thirst is the continuous rectal injection of saline which has already been described. Sips of warm water can be given as soon as the patient can swallow with ease, and a good working rule to remember is to discard the ancient fetish of giving no fluids for twenty-four hours, but to give fluid at once as soon as the patient asks for it, even after gastro-enterostomy.

Sleeplessness after Operations.—Skilful and painstaking nursing will go far to combat this disastrous condition. I have already insisted on the use of electric fans in hot weather, the absence of creaking boards, etc. The patient should be shifted from side to side and tight bandages should be loosened. Ice may well be placed near or on the head. Very often some Benger's food at night half-an-hour before the lights are turned out will produce sleep. In other cases alcohol is the best narcotic. I have known cases where port or champagne will induce sleep, but it must be remembered that in the majority of cases the results of taking these are quite the reverse, and their administration requires great care. In the matter of drugs, morphia should, of course, be rigidly avoided, except if there is agonising pain and no other drugs are found to relieve. Too much stress cannot possibly be laid on the appalling after-effects by giving morphia lightly and unthinkingly. Aspirin, as a general rule, in doses of 10 gr. will produce sleep. If necessary, 10 gr. of aspirin can be mixed with 5 gr. of veronal and given in a little hot whisky. In other cases, a mixture of chloral, trional and aspirin may be given. If a compound of opium must be given, we would advise that 15 to 20 min. of Liq. Opii Sed. be given by the rectum. This is particularly efficacious in abdominal cases.

Pulse and Temperature after Operations.—Let it be admitted that the general appearance of the patient and the pulse-rate are far more important indications than the temperature chart. The normal pulse-rate is usually increased by 20 beats to the minute under an anæsthetic, but it soon drops to normal after the anæsthetic and, during recovery, it may be either increased or diminished as much as 30 beats per minute. It is said that distension alone can put up the pulse-rate. This statement I greatly doubt. It is much safer to assume that if the pulse-rate is increased

mischief is abroad. A pulse-rate of 100 in an abdominal case should always give rise to considerable apprehension whatever the temperature. A sudden and rapid increase of the pulse-rate indicates probable embolism or post-operative collapse of the lungs. Low pulse-rate is probably the result of a stitch abscess.

Temperature.—The usual reactionary rise is up to 100° F. in the first twenty-four hours, but the temperature should be normal within forty-eight hours. Reaction in temperature is higher in bone cases than in cases of hæmorrhage or shock.

Pain after Operations.—This may be due to a variety of causes. The common household flea has been known to give intense torture after operation by its search after food. Again, pins sticking into the patient are not conducive to ease; neither are tight bandages. Again, the use of strong chemical lotions in the wound, of over-tight sutures and tight packing of gauze all cause pain. In abdominal cases, however, it must be admitted that pain after operation varies exactly with the amount of pulling about and exposure of the viscera. The gentle, careful, methodical operator does not have pain in his cases. The dashing and brilliant surgeon may. Very often in abdominal cases pain after operation is entirely due to that curious complaint known by my friend Mr. C. B. Lockwood as "the wind." Of course the personal element in the amount of pain varies largely in different cases.

Methods of Relieving Pain.—If due to pressure of gauze outside the wound, the method of treatment is obvious. Bandages now-a-days can be loosened without the slightest qualms. If the pain is thought to be due to local congestion of the wound, local heat or cold by ice-bags would probably relieve it. A hypodermic of atropin $\frac{1}{100}$ gr. and morphia $\frac{1}{4}$ gr., half-an-hour before operation will greatly decrease the amount of pain, certainly for twelve hours after the operation.

With regard to drugs, aspirin, phenacetin, and trional can all be tried and considered harmless. I would suggest that they be tried in the order given. There is, of course, no other remedy other than general anæsthesia which will relieve intense pain, except morphia.

Use of Morphia.—I have already mentioned that the use of morphia was usually indefensible for mere sleeplessness. It is another matter if its use has to be considered for acute pain. Morphia is usually not absolutely required for this cause. Repeated doses of aspirin will usually relieve bad pain after operation. Morphia, if it is given, should always be combined with atropin. There should be one watchword with regard to the use of morphia in abdominal cases. Before an abdominal operation where there is a suspicion of the case being an "acute abdomen" it should not be given. After the operation it may be given if combined with atropin. The pain of the second and third day after an abdominal operation is usually due to wind and should have been attacked before this time. If no efficacious steps have been taken before this time, repeated turpentine enemas should at once be given. To make a turpentine enema, a drachm of turpentine should be well shaken up in a bottle with 8 oz. of barley-water. This gives less pain and causes less discomfort. In cases where hard fæces are blocking up the rectum, a solution of yeast is by far the best solvent.

In considering the question of pain be it remembered that in all cases of injury to the limbs, muscular spasm is the most constant and distressing cause of pain. This can only be relieved by taking off the splint, changing the position of the limb with the greatest gentleness and rubbing the muscles. The fixed position of a fracture for the first forty-eight hours is rarely forgotten by a patient for the remainder of his life.

Hæmorrhage.—*Recurrent reactionary hæmorrhage.* This comes within about the first twelve hours after operation. If there is a formation of a considerable blood swelling the only treatment is to clean out the wound of the blood clot and endeavour to tie any of the bleeding vessels. If the bleeding point cannot be ligatured, pressure forceps must be left on. If the bleeding points cannot be found the wound should be blocked with gauze soaked with adrenalin. The cause of venous hæmorrhage may often be stopped by raising the bleeding points above the level of the heart. The causes of reactionary hæmorrhage are diverse. Hæmophilia should not be forgotten. Again, in cases of jaundice, the reactionary hæmorrhage is very severe, as, indeed, is the hæmorrhage which occurs during the actual operation. The hæmorrhage may be due to the softening of catgut ligatures or the slipping of ligatures; but, be it admitted, that if the ligatures are uniformly tied after transfixion this cannot occur.

With regard to the treatment by drugs, calcium salts are probably perfectly useless. Adrenalin may be applied locally or Ruspini styptic; an injection of horse serum has been recommended in 5 c.c. doses by Weil.

Secondary Hæmorrhage.—The cause of secondary hæmorrhage is of course ulceration or a suppurating of a wound into the vessels. It may, however, be due to a sort of constitutional diathesis, as in the case of reactionary hæmorrhage. If it occurs, the wound should be opened up at once and every endeavour should be made to find the vessel and put on a forceps

and ligature it if possible. The head of the bed should be raised, the wound opened and ice applied locally. Morphia may be given and saline injected into the tissues, more especially if the bleeding point has been found to the satisfaction of the practitioner.

Internal Hæmorrhage.—The treatment of internal hæmorrhage is obviously to open the abdominal wound in the same way. With regard to the symptoms, increase in pulse-rate is perhaps the most important. Associated with this is very often a considerably raised temperature.

General Treatment after Operations. — Little need be said as to this. There is fortunately a growing tendency not to keep operation cases long in bed. After an abdominal wound has been carefully sutured in layers with durable catgut there can be no reason, it appears to us, to keep the patient in bed in a normal case after the stitches have been removed, and in many cases it is our custom to put the patient on a couch before this time. Despite the usual custom, I doubt very much whether it is necessary for a patient suffering from a radical cure to be confined to the room for more than fourteen days.

In dealing with injuries to joints and fractures, the time must, of course, be necessarily prolonged.

Speaking generally of diet, the sooner the patient gets back to a liberal, mixed diet the better, indeed, to his usual mode of life. It is pitiable to see a patient, one of whose few delights is the abominable habit of smoking cigarettes, having to abstain from smoking for a week or ten days. The motto of both the practitioner and surgeon alike should be to get the patient into a normal and comfortable position as soon as it can possibly be done. One of the surest indications of the suitability of any article of diet is the patient's asking for it.

Posture after an Operation.—This point has already been partially considered. The patient should be kept semi-recumbent, almost in a sitting position, as soon as he recovers from the anæsthetic. Padded boards should be used as already described. The importance of a general massage twice a day during recovery from an operation cannot be too strongly insisted upon.

Treatment of Bed-sores

The most important item in the treatment of bed-sores is undoubtedly their prevention. Fortunately, one of the ethics of present-day nursing is that they *should* be avoided. The occurrence of a bed-sore, whether the nurse is good, bad or indifferent, is invariably considered as a reproach. The rules for the prevention of bed-sores may be considered to be (1) absolute cleanliness; (2) water-beds; (3) the patient being kept in a sitting posture with small variations of position from time to time, with Carson's knee and thigh supports as already described. The commonest cause of bed-sores is ineffective washing and subsequent drying of the skin. Patients' backs after washing should be well and gently rubbed to stimulate the circulation. After this they should be sponged with spirit, methylated spirit being quite effective. There is no advantage in the various strong-scented spirituous mixtures beloved by the nurse. After washing, starch powder and zinc oxide in equal parts should be dusted on. When there is redness of the skin showing an impending bed-sore, the skin may well be painted with Tinct. Benzoin Co., or an ointment as follows may be used—

Ung. Sambuci Viridis, 2 parts
Ung. Alemi, 16 parts
Copaibae, 3 parts.

Post-Operative Insanity

This is now exceedingly rare. It was moderately frequent when double castration was the orthodox treatment for enlargement of the prostate.

In general, it is much more common in septic cases, but, according to Savage, the use of iodoform in such cases had formerly a good deal to do with its origin. The first initial symptom of this form of insanity is usually want of sleep with transient moments of failure to grasp things, or possibly delusions. Such cases may be tided over the dangerous period by medicinal attempts to get sleep. On the other hand, if once a true post-operative insanity has developed, the prognosis is extremely bad.

Coma and Collapse after Operations

At present the risk of post-operative diabetic coma is not a great one and, when necessary, operations on diabetic patients should be fearlessly carried out. They should, however, be operations of urgency, not of mere expediency. Prophylaxis in such cases is of importance. The diet should not be a rigid protein diet, but plenty of food of various sorts should be given. Carbohydrates should be given fairly frequently after the operation, but chief in importance would appear to be the diet used after inhalations of oxygen. My friend, Mr. C. B. Lockwood, has pointed out the results which may follow its use in these circumstances. If the patient remains free from coma for four days after the operation he may usually be considered to be fairly safe.

The treatment of uræmic coma, whether in cases of pregnancy or renal inadequacy, is dealt with elsewhere.

Thrombosis after Surgical Operations

After surgical operations, cases of thrombosis come under one of two headings: (1) clotting in a vein after a traumatic operation on an anæmic person or in one who is the subject of varicose veins; (2) septic clotting in veins in a septic case.

With regard to the first, treatment is naturally to keep the patient at absolute rest with the leg elevated until the clot has become formed or more or less absorbed. If, in addition, there is local inflammation, the so-called "anodyne" belladonna ointment may be applied locally. In my experience, however, the application of a small quantity of "Iodex" on lint will relieve pain rapidly and promote absorption. The possibility of tying the vein above and below the clot may be considered if it is of great importance to the patient to get about. If, however, there is still phlebitis in addition to thrombosis, it would appear to us that surgical procedures are not indicated.

Another form of thrombosis is the so-called "quiet" form rapidly extending along the iliac veins or even into the inferior vena cava. Little is known as to its causation. It usually begins seven to ten days after the operation and is attended by a great liability to bed-sores.

It is well known that aseptic thrombosis is common after typhoid, and is held to be due to an excess of calcium salts in the blood. It is exceedingly doubtful, however, whether the amount of calcium salts has anything whatever to do with it.

The septic form of thrombosis is usually found in the pelvic veins after septic inflammation of the uterus or adnexa. Recently, in such cases, these veins have been ligatured and removed with success.

Rashes

Septic rashes after operations are protean in form, and it is difficult in a general account to differentiate and divide them into various classes. They usually appear one to four days after the operation and are accompanied by a rise in temperature. There is usually a uniform injection of the skin and the rash may be of any appearance, either punctate, morbilliform or papular. The rash is very often associated with albuminuria, and the buttocks and the back of the thighs are most usually affected. Such rashes are common in children and are often considered to be of serious import. The writer's experience, however, is quite different. They rapidly appear and die down. The wound may be perfectly healed or may show signs of sepsis, and, as a rule, the more extensive the rash, the less is the evidence of local sepsis in the wound. This statement does not apply to the late appearing rashes in septic wounds. Here the condition of the wound is very different.

Diagnosis from Scarlatina.—(1) There is no temperature or malaise before the appearance of the rash. (2) The general condition of the patient is normal. (3) The rash is irregular in distribution and character. (4) There is no sore throat. (5) Nor is there any vomiting or severe constitutional disturbance. (6) The rash disappears rapidly and there is no extensive desquamation as in the case of scarlet fever.

Enema Rashes.—These appear three to twenty-four hours after an enema. They are quite irregular in distribution and may be divided into three classes: (1) those appearing in the buttocks and thighs; (2) those appearing in the face; (3) those appearing on the arms and chest. All three classes are usually morbilliform; they are rarely punctiform or urticarial. They disappear in eight to twelve hours and there is usually no fever. Not infrequently they give rise to considerable alarm after an operation on a child, but they should be readily diagnosed.

Ether Rash.—In many children, a few minutes after the administration of ether, there is a profuse, irregular, morbilliform rash over most of the body except the face. This has usually disappeared by the end of the operation and is of no import.

2. Special Treatment

Abdominal Operations.—Here I am not concerned with special surgical procedures, and space will only permit me to give a few general hints as to treatment. In general, an abdominal case should be put quietly and gently to bed and kept in a sitting posture. The nurse will look out for anæsthetic burns on the face and put vaseline on them if found, and at once distribute the blame to the proper source. The same investigation should take place with regard to burns on the extremities. The nurse should be in attendance and the head kept turned to one side until the post-anæsthetic vomiting stage is over. In the case of pain during the first twelve hours, 10 to 15 gr. of aspirin should be given in an enema and no compound of morphia should be given without special instructions. The tube should be passed into the rectum through the sphincters by allowing all flatus being passed twice within the first twenty-four hours and left in for one hour. It is my practice to advise, within thirty-six hours after the operation, that a dose of castor oil should be given followed in three hours by a turpentine enema. If no action is secured by this enema, the state of affairs should at once be considered and active measures taken. No words can properly emphasise the import-

ance of obtaining an early action of the bowels in an abdominal case.

With regard to diet, it is to be remembered that a milk diet is not very good. The patient should be given fluids as soon as ever he asks for them and these be changed in the following order: albumen water, albumen water and milk, milk and soda, Benger, Plasmon, Malt-Glidine and milk, etc. By the third day, once the bowels are open, beef-tea can be given, stimulants and solid food begun. It is a great mistake to either (1) keep the patient too long in bed, or (2) keep him on a milk diet too long.

The average uncomplicated appendix case ought to be on a sofa within five days of the operation and taking a limited mixed diet at the same time. If such be the method of treatment, patients' blessings may not be unheeded by the surgeon.

"The Wind" after Abdominal Operations.—This condition has been known by a variety of names. The above terse name was first used by my friend Mr. Lockwood. The condition is of vast importance, probably the most important condition after operations of all kinds. Put shortly, it means a condition of paralysis of the small intestine with flatulent distension which may be got under rapidly, but which, if allowed to get beyond a certain pass, will kill the patient with all the symptoms of acute intestinal obstruction.

I desire to acknowledge our great indebtedness to my friend for whatever I may have learnt about this condition.

Signs of "the Wind."—Flatus is not passed by the patient within twelve hours after the operation. There is a feeling of discomfort in the abdomen and an accumulation of wind in the intestine which may or may not produce gurgling. Rapidly the abdomen is found to be distended and vomiting begins. The vomiting continues, the distension increases, no wind is passed by the rectum nor is there any attempt at an action of the bowels and, if unrelieved, the condition is soon hopeless.

Cause of "the Wind."—Damage to the intestine or exposure of the small intestine. It is to be observed that the large intestine can be manipulated in almost any way without producing an attack of "the wind." There is a stagnation of the intestinal contents and partial obstruction. Gas is produced by the colon bacillus and also by the B. aërogenes capsulatus. It has been shown that a fluid diet and, more especially a milk diet, produces abundant gas.

We may well remember that a milk diet is not a good preliminary to an abdominal operation and that castor oil is a good preparation. This is of great importance.

Lockwood has insisted on the importance of the presence of peristaltic movements giving rise to "the wind," and he observes that a patient who says she "feels the wind moving" has undoubtedly turned the corner.

Gurgles, whether heard by the ear or by the stethoscope, are of great value, showing that there is peristaltic movement in the intestine, and—to quote again from my friend—"the silent abdomen is of great importance and matters are becoming serious when movement ceases to be heard."

Symptoms of "the wind" are of importance in patients with small and muscular abdominal walls. In weak abdominal walls or where a large abdominal tumour has been removed, we have no reason to fear an attack of "the wind," for in such cases there is a possibility of distension without pressure on the intestine. Again, its onset is not to be feared in operations on the upper abdomen, for these do not involve the small intestine or the mesentery.

Treatment of "the Wind."—Here prevention again is better than cure. An early purgative should be given as already mentioned. A patient should pass flatus by the rectum within the first few hours after an operation. If no flatus is passed within twelve hours, trouble may be expected. Again, post-anæsthetic vomiting should cease in an abdominal case, as a rule, after the smell of the anæsthetic is lost. If it does not, something must be wrong. If no wind is passed within twelve hours, enemata should be given consisting of ½ oz. castor oil, ½ oz. turpentine, and 1½ pints of soap and water. The tube used is an ordinary soft rubber No. 8–10 male catheter, and not a Higginson, and the receptacle used is raised only one foot above the bowel. These enemata are repeated about every three hours until an action is obtained. If no action is obtained after twenty-four hours, 3 gr. of calomel should be given and the contents of the rectum should be tested by an enema after three hours. If there is still no action, 1 gr. of calomel should be given every hour up to 5 gr. Then saline. If this does not produce the desired result, conditions are indeed becoming desperate and heroic doses of purgatives must now be given, such, for example, as 20 gr. of Pulv. Jalapæ Co. or two to three drops of croton oil.

Radical Cure of Hernia.—In the treatment of such cases a few points may be urged. It is most important to keep the patient quite quiet for the first twelve hours, and icebags are useful locally, for not infrequently a certain amount of oozing takes place into the scrotal tissues which ought to be avoided. Retention of urine is not an infrequent complication. As a rule it can be avoided by seeing that the bandages are not too tight. Vomiting is not uncommon. Late vomiting, beginning seven

to ten days after the operation, is often associated with sloughing of the omentum or adhesions. After a radical cure in children under two, no dressing should be applied at all. The wound is kept dry with boracic powder and the child kept on its back with a cradle over it so that no urine gets into the wound.

Genito-Urinary Tract.—The after-care of cases of prostatectomy is now of considerable importance. Universal and hasty removal of the prostate cannot be considered a satisfactory surgical procedure. In many cases where there is foul, septic urine, preliminary drainage of the bladder and administration of urotropin ought to be the course taken. In considering the question of operation, an estimate must first be taken as to the adequacy of the renal function. The amount of residual urine should then be measured in the usual way, and if the bladder is dilated, say, with 20 oz. of residual urine, drainage should be established through a catheter for three days before the opening of the bladder. If the bladder is dilated with foul urine, more particularly if B. coli is present, a suprapubic drain should be established for a week and the bladder washed out with a solution of permanganate of potash, 1 in 500 twice a day. After the removal of the prostate (undertaken with the above preliminary precautions) a large drainage tube about ¾ inch diameter should be put down to the base of the bladder, and this should be washed out every morning with permanganate through the urethra, certainly for the first four days or as long as the bladder continues to be foul. For the first three or four days the urine should be allowed to drain freely into the absorbent dressings; after that a Hamilton-Irving apparatus or Cathcart suction apparatus should be used. Most operators are agreed, however, that for the first few days dry dressings should be used and frequently changed. If the wound does not clear up by the end of the week, it should be sponged out with hydrogen peroxide, and if this does not remove the sloughs, with a solution of Liq. Pepticus. If, at the end of a month the suprapubic wound still leaks, a catheter should be passed and left in for two days. After drainage through the catheter, there may be some epididymitis. This usually clears up soon. After a prostatectomy, a swelling per rectum is often felt at the site of the prostate. This is caused by the dilated vesiculæ seminales.

Hæmorrhage after prostatectomy is to be treated by hot douches, 1 in 5000 of hazeline or silver nitrate, and, if this does not control the bleeding, the bleeding area can be mopped out with 1 in 4000 adrenalin.

Operations on the Rectum.—The surgeon will, after the operation, pack the wound. The first packing should be removed within thirty-six hours of the operation. After that there should be no packing in the sense of pushing gauze into the raw surface, but rather strips of gauze should be placed between the edges of the wound, and these preferably should be smeared with "Iodex." In the writer's opinion, no preparation has at all the same effect in causing healing. The wound should be dressed twice a day, and if there is any pain in connection with removing the dressings, the patient can be placed from the very first in a sitting bath before the dressings are removed. The bowels should not be opened for the first three days after the operation, then a dose of castor oil should be given followed by an enema in the morning. It is important that the patient should not attempt to walk about until the wound is quite healed. The causes for the wound not healing are usually (1) an ineffectual operation; (2) ineffectual drainage; (3) tight plugging; (4) bridging of skin; (5) general constitutional conditions.

Hæmorrhoids.—At the close of the operation a suppository of ½ gr. of morphia should be put into the rectum. Whatever the dressings may be, there is little doubt that a rectal tube should be passed and kept in position for the first thirty-six hours. There is least pain after simple ligature of piles, and less pain after the complete Whitehead operation than the partial one, as the mucous membrane left after the latter often becomes œdematous, extruded and painful. It is usual to give an aperient on the third or fourth night after the operation. I would venture to suggest that the better plan is to give it on the second night, and on the morning of the third day to give an enema. Before the enema, a small amount of cocaine or eucaine can be injected into the bowel. The patient usually complains of no pain whatever once the bowels have been relieved. The usual method at present is to ligature the piles with catgut ligatures and these take care of themselves.

Colotomy.—The wound can be dressed on the second day and the bowel can be opened with a transverse incision about one inch long at the same time. On the tenth day after the operation, the intestine can be completely divided and the belts, etc., can be arranged afterwards.

Operations on the Thorax.—A drainage tube for the first twenty-four hours should be regarded as essential in all major operations on the breast. The patient should be propped up into a sitting position immediately after recovering from the anæsthetic. The arm on the affected side should not be bandaged in. It should be free to move and the patient should be encouraged to move it. The stitches

should be removed in two stages. On the eighth day approximately the first set of superficial stitches may be removed. On the tenth to thirteenth days the deeper stitches may be removed. Great care should be taken in observing the patient and guarding against the occurrence of sepsis. The usual practice is to recommend that if the wound in part shows signs of septic inflammation, the stitches should be cut and removed. I would suggest that in such cases "Iodex" should be applied to the wound from the very first with hot boracic fomentations, and the stitches should only be removed when no improvement is noticed after local applications.

Empyema.—The tube placed in the empyema wound should be short, never long. It should only reach as far as the pleural cavity and never interfere with the expansion of the lung. In young children it is often possible to remove the tube three or four days after the operation, always provided that a sufficiently large tube has been used. In my opinion, the tube should be ½ to ¾ inch in diameter. In adults, a convenient rule for the time of removing the tube may be taken to be the stage when a drachm to two drachms of clear discharge is found. Never wash out the pleural cavity either at the time of the operation or afterwards.

Operations on the Head.—*Hernia Cerebri* is usually caused by unrelieved tension with super-added sepsis. The treatment should be to open up the wound, scrape away the cerebral tissue, which is entirely insensitive and, as a rule, only granulation tissue, and touch it with pure carbolic. In such cases there should be most extreme quiet; the patient should be kept in a dark room, no alcohol should be given and there should be free purging. A long mental rest is necessary after recovery.

Operations on Children.—*Harelip.* It is most important to watch the frequency of respirations after operations for harelip in young children, which in severe cases may be the only indication of the onset of suffocation, owing to the altered conditions in the naso-pharynx and the dropping back of the tongue.

Cleft Palate.—In the author's opinion the best time for an operation on cleft palate is between the third and fourth years. Be this as it may, it is imperative that the patient should have a mouth clean in every respect. Only too frequently cases are sent for operation with a number of septic teeth. The defective teeth should be cleared right away and the mouth allowed to recover. Again, it is important that the child should be kept quiet in its surroundings and used to those who are looking after it. In children's hospitals it is well to keep the children in hospital for a week before the operation. After the operation, for the first forty-eight hours, barley water or albumen water only should be given. After this, each feed should be followed by a good draught of sterilised water. It is most important that there should be no messing about the mouth, which should be left entirely alone for ten days. Parents and hordes of friends should be discouraged in their attentions. Between ten days to three weeks after the operation, according to the surgeon's fancy, the stitches may be removed, which had better be done under an anæsthetic. The occasion may be one of jubilation or the reverse.

Adenoids.—It would almost seem unnecessary to advise that if possible an operation for adenoids should be conducted when the throat is healthy, when there is no nasal discharge or ear discharge and the teeth are sound. The teeth at any rate can always be seen to, but, of course, in many cases the operation is done with a view to checking the nasal or ear discharge. After the operation, the less that is done to the throat and naso-pharynx the better. Naso-pharyngeal sprays of all kinds should be avoided. If the tonsils have been removed a few formamint lozenges may be given to suck. A purge should be given the day after the operation and the mouth washed out with sterilised water after food. If swallowing is very painful after the removal of tonsils, a gargle of Potass. Chlor. 5 gr., Tinct. Ferri. Perchlor. 10 min. to the ounce, will soon relieve it.

Two matters are of great importance: (1) that the period of convalescence should not be unduly prolonged. The operation should be valued at its true worth, *i. e.* a very trivial one. (2) The main factor is change of air. Respiratory exercises carefully kept up and of the simplest character are essential after operation.

Tuberculous Glands of the Neck.—Surgeons are still divided as to whether these cases should be drained or not. I, personally, have given up using a drain, but encourage my patients to lie on the opposite side and keep up some pressure and an ice-bag on the operated side for the first twenty-four hours. There is little doubt that quiet after operations for the first seven days has a remarkable effect on the scar, and the practitioner can well emphasise this fact to girl patients, who can be thus scared into complete quiet. In my experience it is quite unnecessary to keep the patients lying absolutely flat, and I have found that plaster casing is of the smallest possible benefit. Simple bandaging and ordinary reasonable quiet would appear to me to be all that is necessary.

Tracheotomy.—The occurrence of surgical emphysema is to be remembered. Its appearance is most alarming, but it has no influence on prognosis. In the after-treatment of a tracheotomy case it is essential that the

trachea should not be injured and there should be no infection of the lung. In all cases, where it is possible, either in tracheotomy or laryngitis, a soft rubber tube should be used. After the tube has been inserted, the room should be kept strictly at a temperature of 60 to 65° F., and the tube should be sprayed with a solution of bicarbonate of soda (10 gr. to the ounce) to loosen the mucous secretion, and, in cases of diphtheric membrane, to detach it. The tube should be removed at the first possible opportunity. It is better to practise removing the tube too early, even at the risk of having to insert it again, rather than leave it in too long. If it is to be left in for two days, it will be necessary to insert a metal tube.

Treatment of Fractures.—Speaking generally, fractures should never be put in splints and left for more than two days, more particularly when they are near the joint. There is no doubt that splintage in fractures is full of bad effects. If splints are used, they should be removed daily and the injured limb should be moved and gently rubbed, the fractured part being held. The fracture will unite much more readily under gentle rubbing than if left alone. I am far from suggesting that all fractures should be treated by operative measures. A certain number certainly require operation. To define this class is not a little difficult, seeing that it depends very much on the patient's surroundings and the skill of the surgeon. On the other hand, it ought to be admitted that most cases of simple fracture without displacement will do perfectly well if kept in position and gently massaged from the beginning. The point usually lost sight of is this, that the muscles, vessels and trophic nerves are seriously injured in a case of fracture, and their treatment should be most important, whereas the mechanical treatment of a fractured bone is usually the only point thought of. The bone will usually take care of itself. The soft parts are, indeed, the most important element in the case.

Operations on Joints.—It is most important to remember that pain after operations on bones and joints is a very prominent feature, and thus it is well to administer an opiate, as already indicated, at the time of partial recovery from an anæsthetic in all such cases. The patient will then usually be perfectly comfortable if this has been done. For the same reason, all plugging in bone cavities and so forth should be done under an anæsthetic.

In all operations on joints, the one most important factor is that there should be early movement after the operation. The day has now passed when fractures of the patella or cases of opening the knee joint for displacement of the menisci were kept in a splint. In such cases, slow movement is now attempted from the very first and the limb should not be put in a splint at all. The patient should be the judge of the extent of the movements, and will gauge them satisfactorily himself if he has the assurance of his medical attendant that a movement which causes pain is excessive; we find over and over again that a patient with this assurance works his leg continuously so as almost to produce a twinge of pain and prides himself on the increasing ability of his movements.

Two or three days after the operation, it is my practice to endeavour to obtain fairly vigorous movements of flexion through about 40 to 45° in the case of fractures of the patella or removal of the meniscus. In such cases stitches should usually be removed on the tenth day and a collodion dressing put on to support the scar during subsequent movements.

What I have said is still more important in the treatment of injuries in the neighbourhood of the joints. Absence of this treatment has produced bone-setters *et hoc genus omne*.

Treatment of Amputations. — There is little now to say about the after-treatment of amputations. As there is practically no hæmorrhage shock is trivial, except where nerves are cut short. The stump should be elevated after amputation and gently rubbed to avoid spasm of muscles. For the same reason, hot-water bottles should be put round the stump and morphia may well be given. A drainage tube is almost invariably necessary and should be removed in twenty-four hours and a fresh dressing applied.

General Diet.—I would here refer the reader to Dr. Langdon Brown's article in the first part of the volume. From the surgical standpoint, I have already insisted on the fact that the patient's diet should be restored to the normal as soon as possible. I would again repeat that a milk diet, which produces a large intestinal residue and remains in the stomach three and a half hours, and, moreover, is the proper prey for gas-producing organisms in the large intestine, is eminently undesirable. During the period of convalescence, generally the less milk given the better. Albumen water mixed with the white of four eggs in half a pint of water iced and flavoured to the taste would be palatable. After this, clear soups and meat extracts may be considered. Next Benger's Food will probably be found desirable. Eggs, Benger's Food and Malt-glidine will go before more solid foods. The fetish usually observed is to begin with boiled fish—an extremely noxious compound. I would suggest that it is advisable to begin with fried filleted fish or minced chicken and avoid the boiled compounds altogether.

J. K. M.

PART II

AGENTS IN TREATMENT

INTRODUCTION

PHARMACOLOGY is a comprehensive term used to include all exact knowledge pertaining to the action of chemical substances or physical conditions upon the animal body; therapeutics is much more limited in its significance, implying only the art of applying treatment to the patient, an art which may or may not be based on ascertained facts. Modern treatment consists largely in the employment of chemical substances administered or applied to the patient; indeed it would be difficult to find substances which had not been employed as a treatment at some time or another, but those which have survived the test of time are relatively few. Experiments on the living body are the only means we have of obtaining knowledge of the action of drugs and advancing the art of healing. From time immemorial almost up to the nineteenth century practically all these experiments were made upon man, and the number of experiments which have been required before the action of one single drug has been indicated, and the pain and suffering which have been caused indirectly, are beyond calculation. The art of healing made practically no progress till the last century, when science demanded that experiments to be of value must be undertaken with fixed conditions and adequate controls. Soon a small number of drugs became recognised of approved value, but still the *ipse dixit* of a single physician was often sufficient to throw back treatment for many years and do incalculable harm, as for example when a well-known British physician asserted that mercury did only harm in syphilis.

Almost can we assert that the precise action of drugs was never determined by experiments on man because such experiments could not be conducted under precise conditions. For example, such old drugs as digitalis and lead were regarded as circulatory depressants, and prescribed in aneurysms and like conditions until the truth was made patent by experiments on animals. Many therapeutic traditions which are quite untrue find general acceptance even to-day; in spite of the general belief, strychnine and ether have no direct action on the heart. Opium is commonly employed for local application to sensory parts, apparently on the supposition that it depresses sensory nerve-endings; in reality it has no local action of any significance. The hypophosphites are employed because it was thought that they would supply the body with phosphorus and help to build proteins; in reality they are excreted quantitatively in the urine. In this connection it should be pointed out that our British Pharmacopœia is not a compendium of drugs known to have value, but is a compendium of drugs in common use to which a standard is given for the benefit of practitioners. The Pharmacopœia does not necessarily represent approved remedies, but standardised remedies, and so far as it goes it serves as an intermediary between the physician and pharmacist.

The Mode of Action of Drugs

The method by which drugs bring about their several effects in the animal body may be of the simplest or most complicated character. The action of strong sulphuric acid in charring organic matter is the same in living and dead tissues, and depends upon the affinity of this acid for water. The astringent action of the heavy metals, and of the drugs containing tannin, is determined by the fact that they combine with, and precipitate, certain protein substances. Other chemical processes of a more delicate nature than the preceding, which produce effects in the body, may be exemplified by the action of citric acid, which combines with the calcium in the body, forming the not very soluble salt—

$$\begin{array}{l} \quad CH_2.COO\diagdown \\ \qquad\qquad\qquad\quad >Ca \\ CH.OH.COO\diagup \\ \quad CH_2.COO\ Na \end{array}$$

This substance does not ionise so as to liberate the calcium ion, and the specific action of citric acid depends upon its power of removing the calcium ions from the blood.

In any consideration of selective action of drugs on special tissues two important problems must be considered. The first concerns the entrance of the drug into the cell. A drug might reach the blood stream, but for physical reasons be unable to penetrate certain cells in the body and so fail to produce an action on those cells. Tetanus toxin cannot reach the cells of the central nervous system directly through the blood stream, and there is strong presumptive evidence that this is true also of the alkaloid colchicine.

The well-known views of Overton and Meyer seek to explain the selective action of the indifferent hypnotics and narcotics for the central nervous system by their relative solubility in brain lipoid and insolubility in water. More recently Traube has called attention to the tendency of a good many narcotics to produce changes of surface tension and suggests that the narcotic action is dependent on this property. Straub suggests that inhibition of the heart by muscarine is caused by the physical process of the passage of muscarine through the limiting layer of the cell, and that when it has passed this layer it cannot cause inhibition. He finds that in *Aplysia*, muscarine is stored in the heart muscle, and that a certain amount in the outside fluid is necessary for inhibition. If this surrounding fluid is removed, the inhibition is removed. He found, further, in the Selachian heart that atropine delayed the absorption of muscarine, and suggests that atropine in some way alters the limiting membrane, so as to retard the absorption of muscarine below the threshold velocity necessary to produce an action. Here, then, is a true physical hypothesis to account for the selective action of drugs. But even supposing that a drug acts only in the course of its permeation into the cell, due to a difference of concentration inside and outside, this does not explain why strychnine, which is absorbed, does not cause inhibition. In other words, whilst physical factors, as probably all are ready to admit, may be of the greatest importance in limiting the action of a drug, they cannot be credited with determining the specific type of action. It is difficult, for example, to explain on this hypothesis why adrenalin may cause either inhibition or contraction within the same class of tissue cells.

Let us suppose that a drug has obtained access to a cell, the second problem to consider is the change which it brings about in the cell. In the case of narcotics, which is the example we are considering, the hypothesis of Baglioni may be noted; he bases his views on the various groups of benzene phenol derivatives. The amount of paralysis produced by these substances varies inversely with the amount of oxygen present in the side chain, and he concludes that narcotic effects depend on the power to withdraw oxygen from the nerve tissues, or, in other words, that narcosis is a reduction. Herter has shown that chloroform, ether and chloral diminish the oxidising capacity of the tissues. Most of the hypotheses which have been suggested to account for selective action are based on the supposition that drugs combine directly with some constituent of the cell; it will be well to consider what evidence is available in support of this supposition. In the case of toxins it has been definitely shown, first by Wassermann, that the cells of the central nervous system which are known to be affected by tetanus toxin anchor the toxin. But in the case of drugs no such clear proof is forthcoming. Strychnine, like tetanus toxin, has a specific action on the cells of the spinal medulla, and several attempts have been made to prove, by methods similar to those adopted by Wassermann for tetanus toxin, that strychnine acts by combining with the spinal medulla or with one or other of its constituents. Strychnine mixed with an emulsion of spinal medulla shows no evidence of having entered into chemical combination, since it can still be separated from the mixture by means of the ordinary solvents for alkaloids. In this respect, then, it behaves quite differently from tetanus toxin. Furthermore, these observations can be explained more readily in another way than by supposing that the strychnine enters into some form of combination with the spinal medulla. Koch and Mostrum conclude from their experiments that the central nervous system, especially the spinal medulla, by its high phosphatid content, is enabled to absorb the strychnine from the blood stream on account of the affinity of the lecithin and kephalin for the strychnine as compared with serum albumin, but there is no evidence that this attraction of the strychnine by phosphatids is other than physical.

It must not, however, be accepted as a general rule that because an alkaloid exerts a specific affinity for a certain tissue it will necessarily only collect in that tissue, though in many cases it undoubtedly does so. Nicotine, for example, exerts its action on nerve cells when administered by the mouth or injected into the circulation in non-lethal doses; yet Heger and others have shown that it quickly disappears from the blood, and is taken up by the liver, from which it can be obtained by distillation. Indeed, it is now generally admitted that even tetanus toxin may be fixed in other cells besides those on which its activity is most manifest; thus the cells of the liver and spleen, besides those of the brain and spinal medulla, fix tetanus toxin. Many other attempts have been made to show that drugs act by chemical combination, thus Matthews thinks that potassium may combine directly with colloid so that the colloidal complex acts as the anion. Koch and Pike state reasons for their belief that the greater concentration of potassium in the cells of a tissue as compared with the surrounding lymph spaces or serum can be partly explained by a specific affinity of this element for some phosphatids, especially kephalin. These typical examples from a mass of facts show that no conclusive evidence exists as yet, proving that physiological activity produced by drugs is

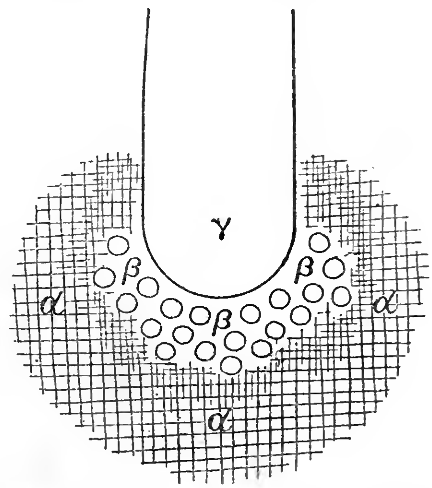
brought about usually by a chemical combination between the drug and the protoplasm of the cell or one of its constituents.

It will be well now to notice briefly the chemical hypotheses which have been advanced to account for the action of drugs. Biologists until recently have been content to accept the giant protoplasmic molecule of Pflüger as a basis upon which to build. The modern biologist must be content to regard the cell rather as a co-ordinated system of ferments, which may be influenced by drugs either by a chemical action on the constituents or by influencing the activity of one or more ferments, at all events until such time as some valid evidence is adduced in support of the giant molecule.

The first hypothesis is that of Ehrlich, who held the view that alkaloids, being foreign to the animal body, were not capable of combining with protoplasm to form such stable compounds as those formed by toxins, but more recently he has laid stress upon the view that drugs which specifically affect tissues are bound to the protoplasmic molecule by certain atomic groupings which he distinguishes from toxin receptors by the term "chemo-receptors." These chemo-receptors are evidently quite distinct from food receptors, and it is difficult to understand how they could arise in an evolutionary world. Langley's view is much the same as that of Ehrlich; he regards tissues as containing receptive substances with which drugs can combine, and these receptive substances may be side chains of the protoplasmic molecule; neither Ehrlich nor Langley gives any idea as to the chemical nature of the receptor. Koch believes that in the living cell two sets of factors must be considered: (1) chemical activities which go on in watery solutions, that is, interaction between non-colloidal molecules, and (2) the control of these by the colloidal aggregates. It is possible that physiological activity in any tissue may be caused by the liberation of a specific hormone, and that drugs may act by greatly increasing or diminishing the production of these bodies, without themselves necessarily taking part in any chemical change, but acting rather as catalytic agents.

Before proceeding to the study of the selective action of drugs on peripheral nerve structures, it may be noted at once that in all nerve-muscle and nerve-gland structures drugs are known to stimulate the end-organ in two distinct ways. They may, on the one hand, produce effects closely simulating if not identical with the effects of nerve excitation, or, on the other, they may produce a different type of effect which is generally more gradual in onset and longer in duration; paralysing agents which remove the action of the drugs of the first group fail to affect that of the latter. For convenience the members of the first group are generally spoken of as acting on "nerve-endings," and those of the second group on end-organs, muscle or gland.

Lucas has employed a method for differentiating the various substances in muscle by determining for each substance the curve relating the liminal current strength to the current duration. In the pelvic region of the sartorius stimulation affects only a single substance (α), which is distributed throughout the whole length of the muscle-fibre and is not affected by curare. The nerve-trunks contain a substance (γ) whose excitatory process is more rapid than that of (α); it is frequently excited when the electrodes are applied to the middle region of the sartorius muscle, and is



Excitatory substances in the nerve-muscle system.

no longer in functional connection with the muscle after weak doses of curare. In the region of the sartorius in which the nerves end is the β substance with its extremely rapid excitatory process; it remains in functional connection with the muscle after enough curare has been given to sever the functional connection with (γ). The experiments show clearly that there must be three different substances in the nerve-muscle system, each of which directly or indirectly can excite contraction (see figure). Thus we have reason to believe that physostigmine and probably curarine act upon the γ; adrenaline, pilocarpine and atropine upon the β; and pituitrin and most metals upon the α.

Methods of Administering Drugs

By the Mouth.—This is generally the most convenient way of administering drugs, and in the

case of drugs which are required to exert a local action on the alimentary canal the only way. Purgatives, anthelmintics, gastric and intestinal astringents which are not required to be absorbed must be given in this manner. For example, bismuth is given for its astringent and protective action on the gastric and intestinal mucous membrane; drugs containing tannin are given because they precipitate proteins; neither of these substances is absorbed.

When a drug is given with the object of being absorbed and producing a specific action, then administration by the mouth has still some advantages over, let us say, the method of injection, because by this means it is possible to obtain a mild degree of action lasting over a considerable time. Many, if not most, drugs are excreted soon after their absorption into the blood, and the specific action is continued just so long as they are being absorbed, so that it is obvious that to obtain a prolonged effect the absorption must be gradual and the drug should therefore be given by the mouth. This general rule is not true of all drugs: a few are absorbed by some tissue or tissues in the body and retained often for days or weeks; such drugs are said to be cumulative, and of these digitalis and lead will serve as examples.

To ensure the most efficient absorption the drug should be given pure: a strychnine solution is absorbed more rapidly than the alkaloid from a tincture of nux vomica, a pure quinine salt quicker than that in Cinchona bark, and so on. The gums, resins and colloids present in the impure drugs retard absorption.

Hypodermic injection is employed when it is required to obtain a rapid specific effect. For this purpose a solution of the drug is used, and the preparation must not be of an irritating nature. The drug diffuses through the tissues in all directions and later reaches the blood stream and exerts its specific action. Sometimes a drug may be injected subcutaneously for its effect on the subcutaneous tissues; absorption is then not desirable, and to limit this the drug may be given with some other drug which constricts the blood-vessels. Cocaine is used in this way as a local anæsthetic, and is often combined with adrenaline to limit absorption.

Some substances are destroyed by the intestinal ferments and must be given hypodermically; such are diphtheria and tetanus antitoxin, tuberculin and hypophyseal extract. Sometimes also normal saline to the extent of many pints is given by this route, as in profound anæmia and shock and puerperal convulsions. If the drug is injected into the substance of a large muscle absorption is very much more rapid than if the injection is into the subcutaneous tissue

Intravenous.—This method is employed generally in emergencies; in threatened death from hæmorrhage normal saline should be injected by this method. Syphilis is sometimes treated by injecting mercury or one of the organic arsenical compounds intravenously. One method of administering ether is to allow a solution of this drug to enter a vein slowly. Most drugs like ether, having reached the blood are free to exert their specific effects immediately, and the effects fade away a very few minutes after the injection. Mercury and arsenic, however, are in some way held by the tissues and are excreted very slowly. Digitalis is sometimes given in this fashion when a rapid effect is desired; but digitalis takes time to act and several hours must elapse before the digitalis action is obvious.

Inhalation is especially convenient when a local effect is desired on the broncho-nasal mucous membrane; the volatile oils placed in hot water may be inhaled in this way. The inhalation of ammonia gas in the form of smelling salts is employed to excite the sensory nerve-endings in the nose and so reflexly to quicken the heart-beat and respiration. The method of inhalation is sometimes used when it is desired to induce a specific action. In this instance the drug, which is necessarily of a volatile nature, is absorbed with great rapidity from the enormous mass of lung capillaries, so that the effect is rapid in onset but soon ceases when the inhalation stops. Amyl nitrite is so used to dilate the splanchnic blood-vessels. Anæsthetics of a volatile nature, such as ether and chloroform, are therefore generally superior to those which are solid, such as chloral hydrate or urethane. The smoke of burning belladonna or tobacco leaves is inhaled to relieve asthma and the fumes of ammonium chloride to relieve bronchitis. Gases such as oxygen and nitrous oxide are given by inhalation.

By the skin several methods are adopted to ensure absorption. The drug may be merely painted on the skin as in the case of iodine or guaiacol, when absorption occurs slowly. Sometimes plasters are used, as in the case of the belladonna plaster; here the atropine is absorbed only very slowly, and the plaster should be left on for at least a week if any considerable degree of absorption is desired. A more usual method is to rub the drug, which must be contained in an alcoholic or fatty basis, well into the skin. Cod-liver oil is sometimes given this way, and this method of inunction is not infrequently employed with mercury when it is desired to get a large quantity of this metal into a syphilitic patient.

By the rectum drugs may be given for a local action, either on some diseased tissue or to

excite the mucous membrane locally and reflexly to empty the rectum. Sometimes they are given that they may be absorbed and exert a specific effect. Absorption from the rectum is as rapid as from the duodenum, and this method of administration is employed when it is undesirable to administer drugs by the mouth, as for example in tetanus.

Nutrient enemata may be useful if they are thoroughly and efficiently pre-digested, the rectum of course having no power of digestion.

Dosage

The dose of a drug for a particular patient should be gauged from the weight of the tissue upon which the drug is required to exert its specific action. But this is not practical, and so the total weight of the patient has been substituted, though it by no means follows that the weight of any particular tissue varies with the total weight of the body. For practical purposes doses are suggested in the Pharmacopœia for average adult patients. Dosage, therefore, is to some extent a question of experience and rule of thumb.

Many conditions must be taken into consideration when choosing the dose of a drug for any particular patient. Age is an important factor; a child clearly should not receive the same dose as an adult, since its weight will be much less. A simple method of indicating roughly the appropriate dose of any drug for a child is to add twelve to the age in years and divide the age by this sum; the figure obtained is the fraction of the full adult dose which may be given. Thus for a child of three years old the dose would be $\frac{3}{3+12} = \frac{1}{5}$ of the adult dose. Many drugs are particularly well borne by children, and doses much in excess of what would be administered by this rule may be given; arsenic, mercury, atropine, purgatives, ipecacuanha are examples: morphine and narcotics, on the other hand, must be given with great caution, and the application of rule of dosage mentioned would give figures dangerously high.

In choosing the dose of a drug its method of administration must be taken into consideration; the dose by the rectum may be twice that given by the mouth, but if given hypodermically the dose should not exceed half that by the mouth. This is an arbitrary dictum which need not receive too close an adherence.

Tolerance and idiosyncrasy (supersensitiveness) receive consideration elsewhere, and clearly these conditions should modify dosage. The time at which a drug is taken may modify its action. Hypnotics should obviously be taken before retiring to rest. Quinine administered for the treatment of malaria must be taken at such a time that the maximum amount of quinine may be in the blood when the spores are liberated, that is to say, when the parasite is most vulnerable. Alkalies administered two hours after a meal will neutralise acid in the stomach, but administered on an empty stomach half-an-hour before food they inhibit for a time the secretion of gastric juice.

By far the most important consideration which modifies the action of drugs is disease. Potassium iodide increases the percentage of iodine in the thyreoid gland, and oftentimes cures goitres by so doing; it facilitates the solution and, therefore, excretion of lead albuminates in lead poisoning; and it ensures the absorption of the caseous material of syphilitic gummata. Clearly it can have none of these actions in health. In acute toxæmias from typhoid fever, diphtheria and other microbial infections, drugs soon cease to exert their ordinary actions on the central nervous system. The respiratory centre is no longer excited by five or even ten grains of caffeine, and large doses of strychnine produce little or no effect; indeed, in severe cases, one-grain dose of strychnine may be quite without any apparent effect, though half a grain is often fatal to a man.

Cumulation is another factor which sometimes influences dosage. Some drugs when administered over a prolonged period are excreted more slowly than they are absorbed and become stored up in certain tissues of the body. When such cumulation has occurred not infrequently there may be a sudden onset of poisonous symptoms. Drugs which may produce these effects are digitalis, lead, sulphonal, bromides and others.

Other factors which must be taken into consideration in prescribing drugs are sex, temperament, fasting, pregnancy.

Some Considerations on the Absorption and Excretion of Drugs

Absorption.—On few subjects in Pharmacology is our knowledge more limited than that which deals with the absorption and excretion of drugs. Why are chlorides absorbed so readily from the alimentary canal, whilst sulphates are refused admission into the body? The answer is unknown, yet in many instances it is just such facts as these which are at the basis of the action of drugs. It is permissible to prescribe the sulphate of iron quite freely by the mouth, because it is known that only a trace of what is administered will be absorbed; indeed, were it all absorbed there would not be so much difference between the specific toxicity of this substance and that of corrosive sublimate. Or, to take another example, were one-tenth part of the usual dose of Epsom salts absorbed

into the system severe cardiac symptoms would result.

Many drugs are given on the assumption that they are not absorbed, and with the object of producing local and reflex effects, and in these instances if absorption should occur evil effects must ensue. The vegetable purgatives afford an example; they contain irritant principles which excite the alimentary canal and induce reflex peristalsis; if, for some unusual cause, they are absorbed, they give rise to renal symptoms and sometimes to nephritis. It is for this reason, among others, that it is advisable to prescribe these drugs in the impure state—that is, with their natural gums and resins—since contamination with such bodies is well known to delay absorption. Anthelmintics and emetics, also, are drugs deliberately chosen for their local action, and not for specific effects after absorption. Many expectorants act in this way: ammonium carbonate, senega, and quillaia will serve as examples; they increase the flow of bronchial mucus by exciting the nerve-endings in the stomach, and so affecting the bronchioles reflexly through the medulla oblongata.

If it is desired that the whole of a dose of some drug shall be absorbed into the system, one plan is to inject subcutaneously, and it is not a matter of indifference as to where the injection is made. Much evidence has accumulated to show that the drug diffuses from the seat of inoculation through the tissues, much in the same way as rings on a pond form as the result of disturbance. The subcutaneous injection of a local anæsthetic such as cocaine shows this perfectly: the anæsthesia, profound at the seat of injection, gradually fades as the distance from this point increases; so that an injected drug produces a pronounced effect on the tissues in the neighbourhood of inoculation as the result of diffusion, and a much smaller effect on distant tissues, since the drug will only reach these through the circulation after absorption. If $\frac{1}{30}$ gr. of strychnine, which acts upon the retinal nerve cells of the eye, be injected into the temporal region of a man the eye on that side is affected; the field of vision, especially for blue, is enlarged and the acuity of vision is increased, but the opposite eye is hardly influenced. This effect must be due to direct diffusion of the drug to the eye, as if it reached the eye through the circulation both eyes would be equally affected.

When a rapid general absorption is aimed at, with the object, let us suppose, of acting on the circulatory system, the seat of injection is still important. Tyramine is one active constituent of the liquid extract of ergot; this amine, when injected into the left forearm of a man (dose 30 mgs.), raised the blood pressure from 122 to 128 mms. of mercury; but the same dose injected round the cellular tissue in the region of the clavicle on another occasion raised the blood pressure from 122 to 138 mms. It would appear, then, to be rational to inject our drug under some portion of the skin as near as possible to the organ or tissue upon which it is desired to act, and where a rapid action is desired to choose some loose cellular tissue.

Many drugs are quite ineffective in their action when taken by the mouth. Calcium salts are only absorbed in healthy people with difficulty and very slowly, so that the calcium content of the blood is hardly altered by taking chalk, calcium lactate, or any other calcium salt by the mouth. Potash and ammonium salts also fail to exhibit their specific actions when administered orally, in spite of the fact that they are very readily taken up into the system. It is well known that potassium in excess is a profound poison to all living tissue, and that ammonium salts in the blood cause convulsions by acting on the medulla oblongata. Nevertheless, these drugs may be taken for all practical purposes in unlimited amounts without causing these effects. The amount of potash salts taken daily by the vegetarian far exceeds anything ever prescribed by the physician. Potassium and ammonium salts owe this absence of toxicity to their property of easy excretion; the rate of excretion can keep pace with that of absorption, so that the amount of the drug in the tissues is not perceptibly increased by the oral administration. The specific effects of these drugs can, however, be obtained by injecting them, when the rate of absorption exceeds that of excretion.

With some drugs considerable delay occurs even after absorption before the desired specific action is obtained. This applies to digitalis and colchicum. Digitalis after absorption is slowly taken up by the muscular tissue, especially that of the heart, and it is not perhaps till two or three days have passed since the introduction of the first dose of digitalis that the patient is under the maximum influence of that dose of the drug. It is for this reason that the treatment of pneumonia by cardiac tonics is started early, so that, should the heart begin to fail, it may be already under the influence of the drug.

A group of drugs which has attracted a great deal of attention in modern times is that of the organic compounds of the metals. Those of iron and arsenic are perhaps the most important, since these are given with the object of being absorbed. The organic compounds of iron possess certain advantages over the inorganic; they are not astringent, and therefore do not upset digestion to the same extent as the soluble inorganic bodies. But it must be

remembered that the combinations of iron with protein, such as the Ferratin of Schmiedeberg, or one of the products prepared from blood, require to be digested before the iron they contain can be absorbed. Furthermore, experimental therapeutic investigations have shown quite clearly that patients suffering from chlorosis improve, as regards the percentage of hæmoglobin in the blood, quicker when they are taking one of the ferrous carbonate preparations than one of these organic preparations. With regard to the organic preparations of arsenic, however, the tale is different, since, unlike the iron compounds, they are readily absorbed. These compounds, so long as they retain the molecular form, that is, so long as the arsenic forms an integral part of the molecule, are non-poisonous in so far as arsenical action is concerned.

From the œsophagus and stomach absorption of chemical substances is practically nil; it is greatest in the duodenum and upper part of the ileum. In the colon a good deal of water is absorbed and in the rectum absorption again is very active. Strychnine convulsions may be produced as easily and rapidly by placing the alkaloid in the rectum as in the duodenum, though of course proteins and substances requiring digestion cannot be absorbed from the rectum and so the old-fashioned undigested nutrient enemata have been shown to be of little if any value, though proteins which have been completely digested to the state of amino-acids may be readily absorbed and act as nutrients.

In concluding this section it may be pointed out that the rate of absorption of drugs from the alimentary canal may be influenced by the administration of other substances, either previously or simultaneously. One example will suffice. Alcohol is not only absorbed with great rapidity itself from the stomach and intestines, but it facilitates the absorption of other substances dissolved in it.

Principles of Treatment

Treatment by the physician is often very unsatisfactory, frequently because either he is asked to treat a disease the pathology of which is unknown, such as gout or epilepsy, or because he is asked to treat not an active disease but a scar left by disease such as may cause the symptoms of mitral regurgitation.

Sometimes, when the exact cause of a disease is known, it is possible to produce immediately a cure or decided relief by the use of a drug, and such treatment is spoken of as specific. We believe that chlorosis is caused by the deficient absorption of iron in the food, and patients suffering from this disease can be cured by the administration of iron either by the mouth or subcutaneously. Goitre is often a compensatory hypertrophy of the thyreoid gland; for some cause the internal secretion is inefficient and the gland hypertrophies to endeavour to supply the needs of the body. This inactive secretion may be due to the deficient absorption of iodine, in which case the administration of iodides to the patient will rapidly produce a cure.

Quinine cures malaria because it destroys the malarial parasites when these are free in the blood. Similarly mercury and arsenic cure syphilis by killing the specific protozoon. Other such examples are the employment of emetine in amœbic dysentery, arsenic and antimony in trypanosomiasis, potassium iodide in actinomycosis and others. Treatment in all these instances may result in a permanent cure. In other cases the cure is only certain so long as the drug is taken: the disease myxœdema is the result of atrophy of the thyreoid gland; the patient is cured by taking thyreoid gland, but remains well only so long as he continues to take the drug. The acidosis in diabetes is due to oxybutyric acid. The body is able for a time to cope with this and neutralise it by ammonia salts, but a day comes when the metabolism is so seriously disturbed that a great diminution in the alkalinity of the tissues ensues, followed by coma. Alkalies relieve this condition for a time; deficient absorption of alkalies will lead in these cases to the onset of coma.

Sometimes, though not commonly now, specific treatment is empirical: colchicum relieves the acute attack of gout, though how it acts we cannot say, as so little is known of the pathology of gout. Salicylic acid cures acute rheumatism, but as we have no certain knowledge of the cause of rheumatism it is not possible to state how the salicylates act. Arsenic cures for a time pernicious anæmia: the pathology of pernicious anæmia is unknown, and, therefore, it is a little difficult to suggest the mode of action of the arsenic in this disease.

The treatment of most patients is in no way specific; we can often remove the objectionable symptoms about which the patient is complaining, whilst leaving the pathological condition untouched. Digitalis and rest may often so alter the condition of a patient who has a failing heart as to simulate a complete cure. An attack of spasmodic asthma may be relieved either by some atropine preparation which relieves the constriction by paralysing the constrictor nerves or by an injection of adrenalin, which excites the sympathetic and stimulates the dilator nerves. The attack is cured, but the cause remains. It is possible indeed to alter the functions of many if not most tissues in the body without interfering with those of

other tissues. It is possible to remove symptoms or to exaggerate them, and in the treatment of a patient whose condition is well recognised pathologically and for whom a definite diagnosis has been made, it should be clearly understood that the physician may none the less take all credit for a recovery even in the absence of specific remedies; he appreciates his patient's condition and the dangers which lie before him and takes the necessary precautions beforehand. For example, many of the deaths in pneumonia are the direct result of cardiac failure; if any likelihood of such a condition were to present itself to the physician he could dose his patient with strophanthus or digitalis some two or three days before the expected crisis, so that at the time it was required it would already be exerting its optimum effect.

Proprietary, Patent and Secret Remedies

Some of the terms in common use first require definition. Quack medicines was a term at one time given to nostrums sold publicly in the market-place before such time as their proprietors became millionaires. The term patent medicine is a misnomer, since, as popularly used, it does not apply to products protected by letters patent under the great seal, but to proprietary remedies recommended in the treatment of disease. Any one is at liberty to make or sell such remedies who pays for the licence, which costs five shillings. A true patent cannot be held as valid unless there is something novel and useful about it, and in no case can a drug or chemical substance be patented, but only the process of its manufacture. It has been decided in the courts of law that if a patent is obtained for the preparation of a certain drug, and if a characteristic name or trade mark is given to that drug, the State grants fourteen years to the proprietors for the sole right of manufacture, after which time the patent lapses with the trade mark, and both become public property.

Proprietary remedies may be divided into (1) secret, for which a stamp duty is fixed, beginning at a penny-halfpenny for each shilling retail price; (2) those in which the composition is disclosed (these escape the stamp duty even when they are recommended for the treatment of certain diseases if sold by pharmacists); and (3) patent medicines proper. The owners of proprietary medicines rarely take out a patent: first, because there is nothing novel or useful in their nostrum; and, secondly, because the formula would have to be published, so they apply to it a distinctive name or trade mark. A trade mark need not apply to anything novel or useful; indeed, the substance to which it applies is frequently some common chemical bought by the proprietor ready made. A trade mark, unlike a patent, does not apply for fourteen years only, but is valid for ever. So that, if a proprietor sells a drug which contains no scheduled poison and no large amount of alcohol, and if it is stamped, he possesses absolute proprietary rights and absolute secrecy for ever.

Proprietary remedies not of a secret nature are those with which the medical profession are mainly concerned; and for the introduction of some of these medical men and the public are indebted to certain of the great manufacturing houses, though naturally it is from the university laboratories that such advances usually come. Adrenalin, antipyrin, arsacetin, chloral, cocaine, veronal, eserin, the nitrites, novocaine, stovaine, strophanthus, are a few of the remedies which owe their introduction to the pharmacological laboratory. Indeed, it is not too much to say that no drug of importance has been introduced into medicine within the last twenty years except through the laboratory. What, then, should a manufacturer do after discovering through the pharmacological laboratory a substance which promises to be useful in medicine, in order to introduce this new drug? He may, of course, take out a patent for the process of manufacture and give the substance a distinctive name, in which case, if his patent is valid, he will have the sole right of manufacture by that method for fourteen years, which is sometimes extended. He may, on the other hand, refrain from taking out a patent and apply to his substance a distinctive name or trade mark which will remain his private property always.

Not infrequently a manufacturer is advised that certain previously unknown therapeutical properties occur in a well-known chemical compound, and after a number of clinical experiments he endeavours to persuade the medical profession to prescribe his substance under the fancy name which he has given it. Other manufacturers follow in the wake and place the same substance on the market under yet other registered names, either devised on purpose, or taken from a number of names previously registered and kept in stock for emergencies. Aspirin, acetysal, xaxa, saletin, salacetin, are some of the names by which acetyl-salicylic acid is known. Aspirin was the original substance introduced into medicine as the result of pharmacological investigations, and around which the literature gathered; the other names are parasitic, and followed later. If a right to use a fancy name is legitimate, this should clearly be confined to aspirin. As an example of old drugs introduced into medicine under new names atoxyl may be mentioned; this was prepared so long ago as 1683 by

Bechamp, and for it numerous fancy names have since been given. The introduction of antifebrin in 1885 for a very well-known chemical body—acetanilid—has also led to much confusion.

Protection and Tolerance

The body has many means by which it can protect itself against the harmful action of chemical substances, vomiting, purgation, rapid excretion, or non-absorption are examples of these; but the most important of these, after absorption into the blood has taken place, is often its destruction. Some of the simplest ways in which the organism protects itself are represented by the aromatic series of drugs. These substances, besides being employed as medicines, are formed from protein breakdown in the alimentary canal, and as some of these are toxic it is obviously important that the body should have some means of protection. Phenols generally become combined with sulphuric acid, and the resulting compound is excreted with ease, and is much less toxic. In poisoning by carbolic acid the available sulphates in the body may be used up in this process of "disintoxication," so that if the urine be examined for sulphates, instead of finding about one-tenth ethereal sulphate and nine-tenths of inorganic sulphate precipitable by barium, the whole sulphate may exist as ethereal sulphate, and the body may be in a state of sulphate starvation. In such cases sulphates should be injected subcutaneously or better intravenously; sulphites act even better than sulphates, but if a really rapid effect is desired in any condition in which phenols are causing poisoning the persulphates should be administered.

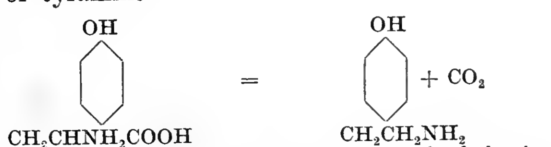
Sometimes aromatic bodies combine with amino-acetic acid (glycocoll) and by this means are rendered non-poisonous. Salicylic acid is excreted partly in this way. If the salicyluric acid (glycocoll salicylic acid) be extracted from the urine of rheumatic patients who are being dosed with salicylates, and be given to other patients suffering from acute rheumatism, it is entirely without action; its therapeutic virtues are no more, and its toxicity is negligible.

Many substances are excreted combined with glycuronic acid. This acid, which differs from glucose only in having a carboxyl group substituted for the terminal primary alcohol group of the sugar molecule, is present in small quantities in human urine combined with aromatic substances, but the administration of camphor or chloral causes it to appear in considerable quantities combined with these substances. Possibly glycuronic acid is an early stage in the oxidisation of sugar, but certain substances foreign to the animal economy may tap this intermediate product, forming a readily soluble and non-toxic substance.

Numerous other methods, though more rare, might be noted of combinations occurring in the body giving rise to non-poisonous compounds; thus furfurol is excreted combined with acetic acid, and amido-benzoic acid with urea.

When the protein molecule is broken down by the action of acid alkalis, or digestive ferments, amino-acids are ultimately produced, and it is in this form that proteins are absorbed; further, it is known that the administration of the final cleavage products of an artificial, sterile pancreatic digestion will serve to preserve nitrogenous equilibrium in an animal as well as the administration of intact proteins.

These amino-acids, of which a considerable number are known, and which vary in kind with the proteins from which they are formed, are non-poisonous substances, and, so far as we are aware, do not give rise to evil results in the animal body. Under the influence of putrefactive organisms they may be altered slightly in composition and become toxic. The simplest method by which the harmless amino-acids are made toxic is by decarboxylation. A few examples will make this clear. Tyrosine may be so changed to para-hydroxy-phenyl-ethylamine or tyramine—



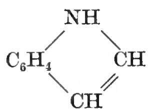
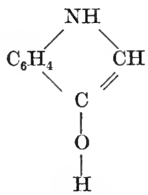
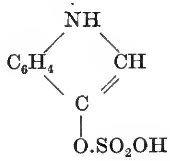
Tyrosine Para-hydroxy-phenyl-ethylamine

Now tyramine is not formed in a sterile pancreatic digestion, but it has been shown that it can be produced in a medium containing tyrosine which has been inoculated with human fæcal bacteria. Tyrosine is then a food substance, but as the result of the loss of carbon-dioxide it becomes poisonous. Histidine is also a normal product of digestion, but the decarboxylated compound is poisonous. A large yield of the poisonous base histamine can be obtained by the action of putrefactive organisms on histidine. Trytophane also can be changed by the agency of putrefactive micro-organisms into its corresponding poisonous amine indolethylamine, and in the same way leucin becomes isoamylamine. In each instance the law holds that the amino-acid is non-poisonous, whilst the base has some toxic properties.

It is probable that putrefaction in the alimentary canal, in some degree, is a normal process, in which case it would be expected that we should find evidence of these poisons in the urine of normal people. Abelous obtained a pressor base from the urine of normal men, which had many of the properties of adrenaline,

and to this he gave the name "urohypertensine." It is probable that Abelous's urohypertensine is iso-amylamine derived from leucine, and nearly all the pressor action is due to a substance which is volatile with steam. A second pressor base can be found in the urine after the complete removal of the first with ether; it is probable that this is partly para-hydroxy-phenyl-ethylamine derived from tyrosine.

Indol and skatol, which are formed during intestinal putrefaction, are oxidised in the body and excreted combined with sulphuric acid, the resulting compound from indol being—

Indol Indoxyl Indoxyl sulphuric acid

The mechanism by which the body can increase its tolerance to a foreign substance may now be considered. Perhaps alcohol, if we can regard this substance as a drug, affords the most familiar example. In moderate doses of, let us say, two ounces absolute alcohol, it is completely oxidised and destroyed; but the rate of oxidation varies in different persons, and as soon as the blood contains somewhere about 0·1 or 0·2 per cent., symptoms associated with the central nervous system become manifest. Those, however, who are addicted to the use of strong beverages may take an amount of alcohol without apparent effect on the central nervous system which would profoundly influence the self-control of the average moderate person, probably because the rate of oxidation is better able to keep pace with the rate of absorption.

It is, however, more particularly in the case of alkaloids that acquired tolerance can be obtained. There is no doubt that morphine is broken up in the body possibly into oxydimorphine, a substance possessing little or no narcotic action. It has been shown after hypodermic injections of morphine into the dog that 70 per cent. can be extracted from the fæces; habituation leads to diminution in this excretion until a stage is reached when daily injections can be given without more than a trace of morphine being excreted. Chemical analysis of the tissues of such a dog shows a complete absence of the alkaloid. This certainly looks as if artificial tolerance were produced in this instance by the increased power of the tissues to destroy the alkaloid.

It is well known that animal tissues *in vitro* possess the power of destroying certain alkaloids. If the tissue juice from the frog's liver, which has been filtered so as to render it entirely free from microscopical particles, be mixed with a little hyoscyamine and kept at 22° C. for two or three hours under suitable antiseptic conditions, the alkaloid disappears. The same effect is obtained in the rabbit, though less marked, whilst the dog's liver shows very little destructive power. The natural tolerance of rabbits to atropine is explained on these lines. These animals, after receiving an injection of atropine, eliminate 15 to 20 per cent. in the urine during a period of from two to three days. But if the animal has been receiving daily injections of atropine for some weeks it is found that after a single large injection no alkaloid is present in the urine after twenty-four hours, nor can it be detected in the tissues after death. The tolerance in this animal would, therefore, appear to be due partly to increased power of destruction by the liver and partly to increased rate of excretion. The natural immunity of the rabbit to atropine depends mainly on its power of destroying atropine and the susceptibility of the cat and dog on the absence of such power; but in all these animals during artificial immunisation the atropine is excreted by the urine more readily.

A small degree of tolerance can also be obtained to nicotine, and this also is caused by the increased rate of destruction of the alkaloid. Oxidation in the tissues is slow, and it can never be accelerated to such a degree that an injection of a poisonous dose of nicotine into the circulation of an animal will lose any large amount of its effect. If nicotine reaches the circulation slowly and in minute quantities it may be dealt with by the tissues, and this is the condition which probably obtains during tobacco smoking. We have strong evidence, then, in support of the view that tolerance means increased rate of destruction, but it must also be remembered that alkaloids may be taken up specifically by certain tissues; thus, when nicotine is injected into the circulation of animals it disappears quickly from the blood and is taken up by the liver, from which it can be obtained by distillation.

The explanation of tolerance for inorganic substances is not so simple. In the case of arsenic it has been found that when arsenious acid was given by the mouth to dogs some degree of tolerance could be obtained, so that by gradual habituation two or even three lethal doses might be administered without producing any severe symptoms, and yet the same dog succumbed if the ordinary minimal lethal dose were injected under the skin. Clearly, then, the drug in these cases is not all absorbed when taken by the mouth. It has been proved that

arsenic eaters can take without ill-effect a dose of arsenic which to a normal man would be fatal. Clinical reports have made it certain that some men can acquire a tolerance which cannot be explained entirely by non-absorption, since instances are not wanting in which large quantities of arsenic have been extracted from the urine. Now if the arsenic be combined directly with a carbon atom ionic arsenic ceases to exist, and all the characteristic properties of arsenic are wanting from the new compound. It is possible that the formation of some such organic compound may be the explanation in these cases, just as some degree of tolerance can be induced with camphor because habituation to this drug gives rise to an increased supply of glycuronic acid; camphor is excreted combined with glycuronic acid and the resulting compound is non-toxic.

Chemical Constitution and Physiological Action

It has long been believed that physiological action induced by a drug must be the direct result of the chemical constitution of that drug; and the relationship between chemical constitution and physiological action has formed the basis of many theses. We have already seen, however, that no reason exists for supposing that drugs enter into chemical combination with the tissues upon which they act, and that sometimes their action depends on their physical properties. It is of no value to argue that their physical properties depend on their chemical constitution, as it is but drawing attention away from the important factor.

Urea, strophanthin and cocaine all paralyse sensory nerve fibrils, and yet no chemical relationship exists between them. On the other hand, the toxicity of yellow phosphorus and the comparative inertness of the red variety can be readily explained by the difference in their physical properties, the greater solubility and volatility of the yellow variety. The curious difference in activity of many stereo-isomeric substances deserves attention. Nicotine, adrenaline, hyoscyamine, and other alkaloids show such isomeric modification, and in each case the dextro variety has little pharmacological action whilst the lævo is very active. The same chemical substance structurally, but with two different configurations in space, has two different actions. It may, indeed, be stated definitely that if the exact chemical constitution of a substance previously unknown is set forth, it is not possible from this fact alone to foretell any of its pharmacological properties.

In many cases it has been noted that the less stable a substance is chemically the more toxic it is. The following series of compounds, showing increasing toxicity, afford an excellent example of this—

$$(CH_3)_3.N{<}\genfrac{}{}{0pt}{}{CH_2.COOH}{OH} \qquad \text{Betaine}$$

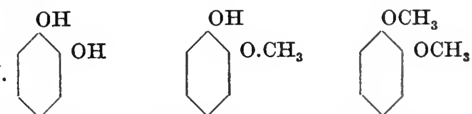
$$(CH_3)_3.N{<}\genfrac{}{}{0pt}{}{CH_2.CH_2.OH}{OH} \qquad \text{Choline}$$

$$(CH_3)_3.N{<}\genfrac{}{}{0pt}{}{CH_2.CHO}{OH} \qquad \text{Muscarine}$$

$$(CH_3)_3.N{<}\genfrac{}{}{0pt}{}{CH{:}CH_2}{OH} \qquad \text{Neurine}$$

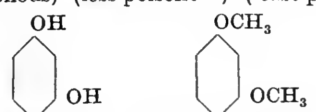
But even this rule has numerous exceptions, for example, cinnamic acid ($C_6H_5.CH{:}CH.COOH$), which is chemically unstable, is, nevertheless, a relatively inactive substance occurring in the natural balsams of Peru and Tolu. Nor does the action of a drug in any way depend upon the chemical changes it undergoes in the body; such highly poisonous substances as strychnine and barium salts are excreted unchanged. In the benzene derivatives we meet with the same difficulties, small changes in constitution produce different types of effect in allied compounds. One example will suffice—

Series I.



Catechol (most poisonous) Guaiacol (less poisonous) Veratrol (least poisonous)

Series II.



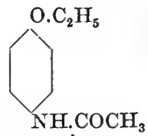
Resorcinol (less poisonous) Dimethyl-resorcinol (more poisonous)

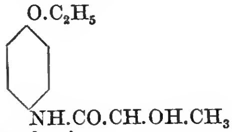
In the case of inorganic salts the degree of action appears to vary with the extent of the dissociation into ions. Potassium ferrocyanide is not poisonous, it has neither the effect of iron nor cyanides and is excreted unchanged; the organic compounds of arsenic, such as the cacodylates and arseno-benzols, in which the arsenic is directly combined with a carbon atom, and which, therefore, do not ionise, have no arsenical properties unless they are broken down and destroyed by the tissues. Perchloride of mercury is easily dissociated in solution and is highly poisonous; mercuric cyanide, though sufficiently soluble, is far less poisonous because its dissociation is so slight. The antiseptic action of metallic salts varies with the degree of dissociation and not with the amount of metal they contain. In the organic compounds much of the pharmacological action is directly dependent on the physical properties of the compound, such as its rate of absorption, volatility and the like.

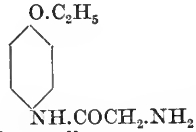
Nevertheless the synthetical chemist from a

correct understanding of the chemical constitution and the action of a well-known drug may, by bringing about small changes in its constitution, so alter its action as to give us another and it may be more useful drug. For example, it has long been known that aniline is oxidised in the body to p-amino-phenol, and on this account the synthetical chemist has produced a large number of aniline derivatives of which phenacetin and acetanilide are official. Some of these are given below—

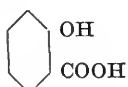

Acetanilide (Antifebrin)

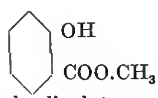

Phenacetin

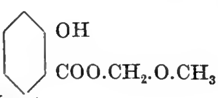

Lactophenin

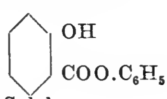

Phenocoll

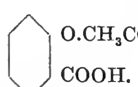
Certain of the derivatives of salicylic acid have proved especially useful. Oil of Wintergreen occurs naturally, and is especially valuable as an external application. Mesotan, also an ester of salicylic acid, is readily split up in the presence of water, salicylic acid and formic aldehyde being liberated. Salol is official, it passes through the stomach unchanged and is saponified by the alkali in the duodenum into carbolic and salicylic acid; its antiseptic action is largely due to the carbolic acid. Aspirin, like salol, passes through the stomach unchanged, but is converted into salicylic acid in the small intestine. It may be a useful substitute for salicylates, especially when these cause gastric symptoms.


Salicylic acid

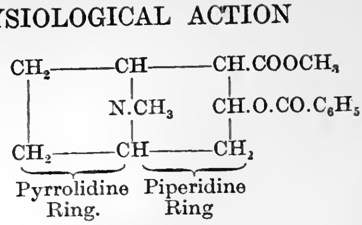

Methyl salicylate (Oil of Wintergreen)


Mesotan

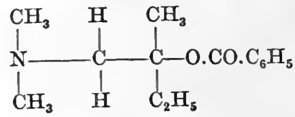

Salol

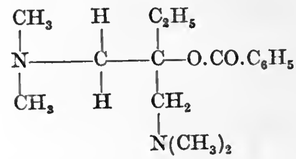

Aspirin. Acetyl-salicylate

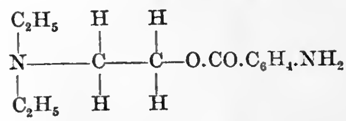
The local anæsthetics are particularly encouraging to the synthetic chemist. Cocaine, the first of this group to be described, has the formula—


Cocaine

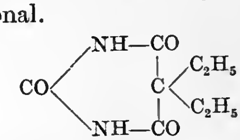
The group $\overset{|}{N}$-$\overset{|}{\underset{|}{C}}$-$\overset{|}{\underset{|}{C}}$-$\overset{|}{\underset{|}{C}}$-$O.CO.C_6H_5$ contained in cocaine also enters into eucaine, and the group $\overset{|}{N}$-$\overset{|}{\underset{|}{C}}$-$\overset{|}{\underset{|}{C}}$-$O.CO.C_6H_5$ forms an integral part of the most recent and valuable of the local anæsthetics, and it is suggestive that sometimes a definite type of chemical constitution may determine a physiological action.


Stovaine


Alypine


Novocaine

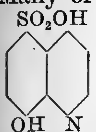
Urea $\left(CO\begin{smallmatrix}NH_2\\NH_2\end{smallmatrix}\right)$ is relatively non-poisonous: it is a diuretic and has very feeble narcotic properties, but many of its derivatives are used in medicine. For example, Bromural $CO\begin{smallmatrix}NH_2\\NH.COCHBr.CH(CH_3)_2\end{smallmatrix}$ has been employed as a mild hypnotic. Urea derivatives of organic acids or ureides are also largely used as hypnotics, perhaps the commonest being diethyl-malonyl-urea or veronal.



Some derivatives of thio-urea $CS\begin{smallmatrix}NH_2\\NH_2\end{smallmatrix}$ are also in common use. Allyl-thio-urea $\left(CS\begin{smallmatrix}NH_2\\NH.CH_2.CH.CH_2\end{smallmatrix}\right)$ or thiosinamine acts as a mild narcotic, though it is used mainly on account of its alleged action in removing scar tissue.

Many substitutes have been invoked for the iodides, but for the most part these are not preferable to potassium iodide. Iodopin, for

example, is a combination of an unsaturated oil with iodine: the iodine is liberated slowly in the body and the compound is often used subcutaneously. Iodoform (CHI_3) has a host of substitutes, each with the object of producing a compound having the same effect but without the odour of iodoform; none of these are, however, equal in effect to iodoform. Euphoren $C_6H_2\begin{cases}C_4H_9\\CH_3\\OI\end{cases}$ gives up iodine to the body like iodoform, but it contains less than one-third of the amount contained in the latter substance. Many of the so-called substitutes like loretin,



, iodo-salicylic acid and sozo-iodol yield no iodine and are, therefore, in no sense substitutes for this drug. W. E. D.

PHARMACEUTICAL PREPARATIONS

Most drugs are unsuitable for administration in the crude state, and it is the duty of the pharmacist to prepare them for medicinal use. The pharmaceutical preparations of the British Pharmacopœia may be grouped into the following classes: tinctures, solid and liquid extracts, juices, infusions, decoctions, liquors, waters, syrups, spirits, wines, vinegars, glycerins, collodions, confections, plasters, hypodermic injections, eye discs, liniments, lotions, mixtures, pills, compound powders, lozenges, suppositories and ointments. In addition to the foregoing classes there are a number of unofficial forms in which drugs are exhibited for internal and external use, as, for example, emulsions, linctuses, compressed tablets, bougies, pessaries and pigments.

Solvents

The most frequent preliminary treatment of a vegetable drug is the extraction of its active principles by means of some suitable solvent, while the chemical substances used in medicine are most commonly administered or applied in the form of a solution.

Water is the most useful of all the solvents, and it has a more extended use than any other liquid.

The "aquæ" of the British Pharmacopœia are used chiefly as vehicles for the administration of medicines. Camphor water and chloroform water are solutions of these substances in distilled water; the remainder of the waters are made by mixing a volatile oil or some part of a plant with ordinary water and submitting the mixture to distillation.

Infusions are aqueous preparations mostly made by macerating a vegetable drug for fifteen minutes in boiling water in a closed vessel, and then straining off the liquid from the residue of insoluble drug. Infusion of calumba and infusion of quassia are made with cold water.

Decoctions are made by boiling a vegetable drug with water, straining and pouring sufficient cold water through the strainer to make up to a given volume.

The liquors form a large and important group. Some are aqueous solutions of volatile substances, as, for example, Liquor Ammoniæ, others are weak solutions of perfectly stable but potent substances, the use of such solutions overcoming the necessity of continually weighing minute quantities. Liquor Hydrargyri Perchloridi is an example of this class. A number of the liquors are made with a solvent other than water.

The lotions, the mixtures and the syrups are all aqueous preparations. The syrups are solutions of various drugs nearly saturated with sugar.

Alcohol as a solvent is next in importance to water, and it has an advantage over water by the fact that alcoholic preparations keep almost indefinitely, whereas aqueous solutions of many organic substances quickly become a medium for the growth of bacteria and fungi. Alcohol is more useful generally than water for extracting the active principles of vegetable drugs; alkaloids, glucosides, resins and volatile oils are soluble in alcohol, while it does not dissolve starchy, mucilaginous, albuminous and other inert principles—a negative character of considerable usefulness.

The medicinal extracts consist for the most part of concentrated preparations of the active principles of vegetable drugs. Some of the extracts are solid, others are liquid; the bulk of them are made by exhausting the drug with alcohol.

The tinctures present the active constituents of one or more drugs in alcoholic solution; the majority of them are made by percolating the drug or macerating it with alcohol of some definite percentage strength.

The spirits are either solutions of substances, such as camphor or chloroform, or volatile oils, such as oil of peppermint and oil of nutmeg in strong alcohol, or they are liquids, such as Spiritus Ammoniæ Aromaticus and Spiritus Ætheris Nitrosi, the preparation of which involves somewhat complicated processes.

Glycerin is a useful solvent, but its range is not so great as either water or alcohol. A glycerin solution is viscous and is useful for local application; in the case of throat paints the glycerin acts as a demulcent in association with the dissolved medicament.

Diluted glycerin is frequently the solvent used in the preparation of non-alcoholic tincture substitutes.

Acetic Acid is an efficient solvent for exhausting many of the vegetable drugs, and is used as a menstruum for making non-alcoholic preparations resembling tinctures, but its acidity is an objection to its general use.

Ether is a solvent for oils, fats and resins, and most of the alkaloids are dissolved by it. Collodion is a solution of pyroxylin in a mixture of ether and alcohol. Acetone, chloroform, benzene and xylol, are similar in their solvent properties to ether.

Olive Oil is used as a solvent of camphor in the preparation of Linimentum Camphoræ.

Almond Oil is used as a solvent of phosphorus in the preparation of Oleum Phosphoratum.

Standardisation

It is essential that the preparations of crude drugs, particularly those prepared from the more potent drugs, shall be always of uniform strength, and since the crude drug may contain variable quantities of active principle, or combination of active principles, an assay process for each of the potent drugs is necessary. This is particularly necessary with preparations of belladonna, hyoscyamus, cinchona, ipecacuanha, aconite, nux vomica, opium and jalap. The preparations of the first four are standardised to contain a definite percentage of total alkaloid, the preparations of aconite are standardised in terms of ether-soluble alkaloids, nux vomica preparations are standardised for their strychnine content, opium is standardised for its morphine content, while jalap is standardised for resin.

Other potent drugs such as colchicum, hydrastis and male fern also can be standardised by chemical assay, but it is generally agreed that digitalis, ergot and Indian hemp can only be satisfactorily standardised by physiological tests.

Standardised "galenical" preparations are unmistakably more satisfactory than preparations the only guide to the strength of which is that they have been made from a definite quantity of a crude drug, but it must be remembered that even standardised preparations may vary in activity in consequence of the presence of constituents which are not usually determined and yet probably modify the action of the chief constituent. The only way in which it is possible to obtain remedies of invariable and constant strength is by the use of isolated active principles, instead of "galenical" preparations, although so far there is very little actual knowledge available as to whether the therapeutic value of a solution of the active principle of a drug is equal to that of a "galenical" preparation standardised to contain the same amount of active principle.

Jowett (*Pharmaceutical Journal*, March 15, 1913) has divided a number of important drugs into four classes.

1. Those where our knowledge is sufficient to warrant the statement that the "galenical" preparation can be replaced adequately and advantageously by the active principle, or combination of active principles, *e. g.* jaborandi, physostigma, coca and ergot.

2. Those cases in which, although the active principles have been isolated and investigated, there is still doubt as to whether these represent the full activity of the "galenical" preparations. Opium, cinchona, belladonna, and hyoscyamus are examples of this class.

3. Drugs whose pharmacological action can be accurately ascribed to one or more active principles, but where the presence of pharmacologically inactive substances affects the physical properties of the active principles so as to give the "galenical" preparations advantages not possessed by solutions of the active principle, *e. g.* nux vomica and digitalis.

4. Drugs whose pharmacological action cannot be ascribed to any principles which have been isolated therefrom, *e. g.* purgative drugs generally and Indian hemp.

Jowett draws the conclusion that only in a few cases is there the necessary pharmacological and clinical evidence that galenicals honestly prepared from drugs of good quality and standardised if practicable, can be adequately and efficiently replaced by active principles, yet in the light of further investigation probably the ultimate end will be the use of active principles on account of their greater certainty.

Drugs possessing little or no Therapeutic Activity

There are a number of substances of considerable importance to the physician and the pharmacist which have practically no therapeutic activity and yet are in constant use. In addition to distilled water there are various flavouring and colouring agents, the suspending agents and excipients, and also the demulcents and emollients.

Flavouring Agents

The flavouring of medicines is frequently neglected, and many good formulæ have failed to compete with preparations of proprietary origin because their flavour has been unsatisfactory. In the British Pharmacopœia there are a number of waters, infusions, spirits, syrups and tinctures suitable for flavouring purposes, while glycerin and gluside may be used as sweetening agents. The waters and infusions are intended to be used as vehicles

instead of distilled water, but fresh infusions should always be used, since concentrated infusions present little or none of the aroma of the drug from which they are prepared. From ten to twenty minims of a tincture, spirit or elixir are usually sufficient to flavour a single dose, while one fluid drachm of glycerin or any of the syrups will be required for each fluid ounce of a mixture.

Bitter-orange Peel is used in several of the pharmacopœial preparations, and affords one of the best flavours for covering the taste of nauseous drugs. Infusum Aurantii and Infusum Aurantii Compositum are good vehicles for bitter tonics. The compound infusion is made from a mixture of bitter-orange peel, fresh lemon peel and cloves. Tinctura Aurantii is made by macerating fresh bitter-orange peel in alcohol; Syrupus Aurantii is made by mixing tincture of orange with syrup; Syrupus Aromaticus is made by mixing tincture of orange with syrup and cinnamon water; Elixir Aurantii is made by dissolving oil of bitter-orange in alcohol and adding syrup and cinnamon water; Tinctura Aurantii Dulcis is made from sweet-orange peel.

Orange-flower Water is distilled from the flowers of the bitter orange; Syrupus Aurantii Floris is made by dissolving sugar in undiluted orange-flower water and then adding syrup.

Lemon Peel in the fresh condition is used for the preparation of Tinctura Limonis and Syrupus Limonis. Syrup of lemon contains lemon juice, hence it is suitable only for mixtures in which the presence of an acid is of no consequence. It is incompatible with alkaline mixtures and mixtures containing a salicylate or a benzoate.

Ginger and Capsicum are suitable flavouring agents for saline purgative mixtures. Tinctura Zingiberis, Syrupus Zingiberis and Tinctura Capsici may be prescribed.

Cardamom Seeds in conjunction with caraway fruit, cinnamon bark, cochineal and glycerin are used to make Tinctura Cardamomi Composita, which is a very popular carminative, flavouring and colouring agent.

Cinnamon Bark distilled with water yields Aqua Cinnamomi, which is a useful aromatic vehicle. Tinctura Cinnamomi and Tinctura Cinnamomi Composita are also used. The compound tincture contains cinnamon bark, cardamom seeds, long pepper and ginger.

Cloves are used to make Infusum Caryophylli and Aqua Caryophylli. Both preparations are good vehicles for alkaline mixtures.

Caraway Fruit is used to make Aqua Carui, which when sweetened is a good and agreeable vehicle for children's mixtures.

Chloroform is in constant use as a flavouring and preservative agent with carminative properties in the form of Aqua Chloroformi and Spiritus Chloroformi.

Oil of Peppermint distilled with water yields Aqua Menthæ Piperitæ, which is a convenient vehicle for stomachic and purgative mixtures, especially those containing rhubarb and magnesium sulphate. Spiritus Menthæ Piperitæ contains 10 per cent. of oil of peppermint dissolved in alcohol.

Oil of Bitter Almond is a favourite flavouring agent for emulsions of cod-liver oil and extract of malt with cod-liver oil.

Vanilla is best prescribed as Tinctura Vanillæ.

Refined Sugar is the most universal sweetening agent; it is used in the preparation of all the syrups.

Glycerin may be used instead of syrup, and is especially useful for preparations of cascara and cinchona, which it renders more easily miscible with water.

Gluside is used as a sweetening agent when sugar is undesirable. Elixir Glusidi (syn. Elixir of Saccharin) is the best preparation. Five minims usually is sufficient to sweeten each fluid ounce of a mixture.

Liquid Extract of Liquorice is especially useful for disguising the taste of the iodides, ammonium chloride, liquid extract of cascara, aloes and paraldehyde. It must be prescribed only in alkaline or neutral solutions; in acid mixtures the flavour of the liquorice is lost, and an unsightly deposit is formed.

Cherry Juice is prepared by pressing a mixture of red and black cherries. Syrupus Cerasi is made by dissolving sugar in the juice.

Mulberry Juice is used to make Syrupus Mori.

Currant Juice, made by pressing a mixture of red currants, and red and black cherries, is used for the preparation of Syrupus Ribis Fructus.

Martindale has suggested the use of a series of "Glyl" and "Syl" flavouring agents, which are solutions of various essential oils, pleasant to the taste, in glycerin and syrup respectively. The flavourings are all of uniform strength, and contain 1 part of essential oil dissolved in 500 parts of glycerin or syrup. Martindale has found especially useful the Glyl and Syl preparations of the oils of bitter almond, coriander, lavender, peppermint and rose, and the Glyl preparations of the oils of bitter orange, cinnamon, pine and thyme.

Colouring Agents

The appearance of mixtures, gargles, mouthwashes and other preparations may be frequently improved by the addition of a suitable colouring agent.

Red.—The most extensively used colour is red in its various shades from coral-pink to a deep crimson red, and a considerable number of preparations are available.

Cochineal imparts a rose-pink or crimson colour to neutral and alkaline liquids, but it is not satisfactory in acid solutions, which turn it scarlet and render it fugitive. It is used to colour Tinctura Cardamomi Composita and Tinctura Cinchonæ Composita. Tincture of Cochineal (Tinctura Cocci) tends to form a cloudy mixture with water, owing to the precipitation of fatty material.

Solution of Cochineal (Liquor Cocci) is a better preparation, it mixes more readily with water, and imparts a more brilliant colour than tincture of cochineal.

Glycerin of Cochineal (Glycerinum Cocci) may be used if the presence of alcohol is undesirable.

Carmine is the red colouring matter of cochineal, and is used to colour tooth powders, dusting powders, and many other toilet preparations. Liquor Carmini is an ammoniacal aqueous solution of carmine, and is a good preparation for colouring alkaline or neutral mouth washes and mixtures. Three or four drops to each ounce of liquid is sufficient.

Cudbear is a purplish-red powder obtained from the lichen, *Roccella tinctoria*. Tincture of Cudbear (Tinctura Persionis) is especially useful for imparting a red colour to acid liquids, and is used in the preparation of syrups having an acid reaction.

Red-Rose Petals are obtained from the red or Provence rose, *Rosa Gallica*. Acid infusion of roses (Infusum Rosæ Acidum) is a convenient vehicle for gargles containing alum or tannic acid; it should not be prescribed with borax or other alkaline salts.

Liquid Extract of Rose (Extractum Rosæ Liquidum) is a valuable colouring agent for acid mixtures in the proportion of fifteen minims to one fluid ounce of the mixture. It is an acid preparation, and alkalies change the fine red colour to a murky green.

The so-called "Liquor Rosæ Dulcis" supplied by manufacturers is usually prepared from cochineal or carmine.

Syrup of Rose (Syrupus Rosæ) is a good flavouring as well as colouring agent.

Red-Poppy Petals are obtained from *Papaver Rhœas*, which grows abundantly throughout Europe. Syrup of Red-Poppy (Syrupus Rhœados) is a frequent ingredient of cough mixtures.

Red Sanders Wood is the heart wood of *Pterocarpus santalinus*. The colouring matter is insoluble in water, but yields a blood-red colour with alcohol. The colour is precipitated by mineral acids.

Compound Tincture of Lavender (Tinctura Lavandulæ Composita) contains red sanders wood.

Alkanna Root, the root of *Alkanna tinctoria*, contains a fine red colouring matter, readily soluble in oils. It is used for toilet preparations of an oily or spirituous nature.

Yellow.—Apart from the use of aniline dyes, a yellow colour can be best obtained with saffron.

Saffron consists of the dried stigmas and tops of the styles of *Crocus sativus*.

Tincture of Saffron (Tinctura Croci) is a good preparation and retains its colour well. About twenty minims should be used with every fluid ounce of the mixture.

Glycerin of Saffron (Glycerinum Croci) is prepared by digesting saffron in a mixture of glycerin and alcohol. Ten minims of this preparation is sufficient for every fluid ounce of mixture.

Syrup of Saffron (Syrupus Croci) is made by mixing glycerin of saffron with syrup. One fluid drachm should be used with every fluid ounce of mixture.

Turmeric is the dried rhizome of *Curcuma longa*. Tincture of Turmeric (Tinctura Curcumæ) may be used as a colouring agent, but the colour is fugitive, and is turned brown by alkalies.

Brown.—A brown colour is best obtained by the use of ordinary caramel or burnt sugar.

Burnt Sugar (Saccharum Ustum) is prepared by heating cane sugar at about 180° C., until a black viscid mass is formed, which is then mixed with about its own weight of water. When mixed with preparations containing a considerable proportion of alcohol, some of the caramel is apt to be precipitated.

Suspending Agents

Substances that are insoluble, or only slightly soluble, in water may be dispensed in mixture form if some suspending agent be added so that the substance is readily diffused when the bottle is shaken.

Mucilage of acacia, mucilage of tragacanth and compound tragacanth powder are the most commonly used suspending agents. Glycerin and syrup are also useful because they tend to make the menstruum more viscous.

In practice, the insoluble substance is rubbed to a fine powder in a mortar, and triturated with a little water to make a thin, smooth cream, the suspending agent is then added, the mixture is diluted with more water and then transferred to the bottle.

Insoluble substances of low density, such as magnesium carbonate, do not need the addition

of a suspending agent. Reference is made in the section on physical incompatibility to the suspension of resin precipitated when a resinous tincture is added to water.

Pill Excipients

In the preparation of a pill mass it is usually necessary to add some material which will bind together the ingredients into a plastic condition.

Among the moist excipients, syrup of glucose, glycerin of tragacanth, manna and confection of roses, are frequently used, while powdered curd soap, powdered liquorice root, gum acacia and tragacanth, are useful absorbent substances. A mixture of hard and soft paraffin, stiffened with kaolin, is the usual excipient for phosphorus, potassium permanganate, and silver nitrate, which cannot be massed with a readily oxidisable excipient.

When the prescriber is doubtful as to what is the most useful excipient for a particular combination, he should leave the choice to the pharmacist, who will then be able to use the material to which he is most accustomed.

Demulcents

A demulcent preparation is one that has a protective and soothing effect when applied to an inflamed mucous membrane. Usually the term is restricted to preparations intended for internal use.

Gum acacia is soluble in water, forming a viscid solution; tragacanth is only partly soluble in water, but swells and forms a gelatinous mucilage. Both preparations are used as demulcents. A gum acacia and cane sugar basis is used to make glycerin pastilles, voice jujubes, delectable jujubes and other preparations supplied by the medical confectioner. A gelatin and glycerin mixture also is used as a demulcent basis for medicated pastilles. The glycogelatin of the British Pharmaceutical Codex contains 12½ per cent. of gelatin, 50 per cent. of glycerin and 5 per cent. of sugar, and is flavoured with citric acid, oil of lemon and orange-flower water, and is coloured with solution of carmine. Most medicaments may be dissolved or suspended in this basis; but tannic acid, extract of krameria, kino and eucalyptus kino are incompatible with gelatin, and must be combined with an acacia basis.

Marshmallow root contains from 25 to 35 per cent. of mucilage, and may be prescribed in the form of a decoction of the peeled root, or as a syrup made by dissolving sugar in an infusion of the root. Guimauve pastilles are a useful and pleasant demulcent; they are made by dissolving gum acacia and sugar in an infusion of marshmallow root, and evaporating the mixture to a syrupy consistence, afterwards adding white of egg beaten up with orange-flower water.

Liquorice root contains glycyrrhizin, a mixture of the calcium and potassium salts of glycyrrhizic acid, also sugar and a large quantity of starch. The dried root yields from 20 to 25 per cent. of an aqueous extract, which is used in the preparation of various lozenges and pastilles in combination with expectorants and sedatives.

Linseed contains from 30 to 40 per cent. of fixed oil, while the epidermis of the seed coat contains a large amount of mucilage. Linseed "tea," made by boiling the whole seed with water, contains the mucilage which is readily dissolved.

Sweet almonds contain about half their weight of a bland fixed oil, and about 20 per cent. of proteids. A demulcent mixture is made by triturating with water a compound powder made by mixing sweet almonds, coarsely powdered, with sugar and gum acacia.

Emollients

An emollient preparation is one that is applied to the skin to protect and soften it and render it more pliable. Emollients are usually of a fatty or oily nature, and they may be classified into—

(*a*) The animal fats, such as lard (adeps), wool fat, beeswax and spermaceti.

(*b*) The vegetable fats and oils, such as oil of theobroma, almond oil and olive oil.

(*c*) The petroleum products, which are obtained from the crude oil produced by the destructive distillation of shale. Soft paraffin is unoxidisable and does not become rancid, but it is not so readily absorbed through the skin as the animal and vegetable products. It may be obtained white or yellow. Soft paraffin is known in this country as Paraffinum Molle, in the United States as Petrolatum, and also under various trade names such as Vaseline, Chrisma, Geoline and Fossiline. Hard paraffin and liquid paraffin also are used in the preparation of ointment bases.

Toilet emollient ointments formerly were prepared by digesting various flowers, such as elder flowers, in mixtures of lard, wax and spermaceti; these are now out of fashion, and even cold cream, made by mixing beeswax, almond oil and a little borax with rose water, has given way to numerous "skin foods," "massage-creams" and "vanishing creams."

The "skin foods" supplied by beauty specialists usually are made with a basis of casein precipitated by adding a dilute acid to separated milk. Casein in a moist condition

is readily absorbed by the tissues, and it is used either mixed with a little glycerin and perfume, or it is combined with a moderate proportion of almond oil.

Vanishing creams are made either with casein or with sodium stearate. Witch-hazel snow or foam—Pasta Hamamelidis—is a sodium stearate preparation. It is made by melting stearic acid and adding to it a hot aqueous solution of sodium carbonate; as soon as all the carbon dioxide had been driven off, solution of hamamelis is added, and the mixture is stirred until it cools and becomes opaque and foamy. A little liquid paraffin is contained in the Codex preparation, in other formulæ glycerin is added, and sometimes also a little wool fat.

Glycerin is a valuable emollient, but should be diluted with one or two volumes of rose water. Glycerin of starch is also used; it is made by mixing starch with glycerin and water and heating until a thick translucent jelly is formed. Starch is insoluble in cold water, but with boiling water it forms a gelatinous mucilage which is used as the basis of many enemata. Starch also forms the basis of violet powder, and many other dusting powders which are applied to the irritated conditions of the skin or slight abrasions in order to protect these from the air and from contact with the clothes or other sources of pressure.

R. R. B.

THE GENERAL PRINCIPLES OF INCOMPATIBILITY

A practical course of training in extemporaneous pharmacy at a dispensing counter is of considerable value to a medical student, but it is seldom that he is able to devote sufficient time to master more than the mere rudiments of the art, hence a medical practitioner may be quite well aware of the drugs that should be prescribed for a particular case, but in consequence of a scanty knowledge of the possibilities of dispensing he may hesitate to write his prescription lest he may combine substances which are incompatible.

Incompatibility may be defined as any unintentional change which interferes with the elegance, usefulness or safety of a prescription. Substances are chemically incompatible when they react on one another, causing precipitation or some unexpected chemical change, and they are said to be physically incompatible when they are immiscible or when a substance in solution in one liquid is thrown out of solution by the addition of another liquid in which it is insoluble.

Therapeutic incompatibility belongs to the province of pharmacology and therapeutics.

Chemical Incompatibility

The subject of chemical incompatibility may be dealt with by giving a detailed list under each drug of the substances with which it is incompatible; such lists, however, are difficult to commit to memory and retain, while many of the incompatibles are very unlikely to be prescribed, hence they are unimportant and mention of them tends to obscure the important examples. In avoiding chemical incompatibility it is better that the prescriber should bring his knowledge of chemistry into play, and in the following pages an attempt is made to indicate broadly the commoner types of chemical incompatibility which should be avoided.

1. The Precipitation of an Insoluble Substance from a Mixture of two Solutions.

Examples.—The soluble salts of calcium, strontium, iron, magnesium, mercury, lead, zinc, copper and silver yield an insoluble precipitate with a number of substances.

Calcium and Strontium.—The soluble chlorides, bromides and lactates of calcium and strontium give a precipitate with the hydroxides, carbonates, sulphates and phosphates of sodium, potassium and ammonium, and with aromatic spirit of ammonia. Avoid calcium chloride with magnesium or sodium sulphate.

Iron.—The soluble iron salts—ferrous sulphate, ferric chloride—form a precipitate with the hydroxides, carbonates, benzoates and phosphates of sodium, potassium and ammonium, and with aromatic spirit of ammonia. Ferrous sulphate and potassium carbonate precipitate green ferrous carbonate, a reaction intentionally made use of in making Mistura Ferri Composita.

The scale preparations Ferri et Ammonii Citras and Ferri et Potassii Tartras are not precipitated by alkalies in the cold, but they are incompatible with dilute acids. From Ferri et Quininæ Citras, the alkaloid quinine is precipitated by admixture with the alkalies.

Magnesium.—A solution of magnesium sulphate will give a precipitate with the soluble hydroxides, carbonates and phosphates, but not with bicarbonates and ammonium carbonate. Magnesium sulphate may be prescribed, therefore, with sodium bicarbonate and ammonium carbonate.

Mercury.—A solution of mercuric chloride is precipitated by the carbonates, bicarbonates and hydroxides of sodium, potassium and ammonium, also by lime water and all preparations which are strongly alkaline in their reaction. The oxides and iodides of mercury are insoluble. Red mercuric iodide is precipitated by potassium iodide, but is soluble in excess of the potassium salt, and solution of mercuric

chloride is frequently prescribed in this combination. Lotio Hydrargyri Flava contains finely precipitated mercuric oxide, and is prepared by adding lime water to mercuric chloride. Lotio Hydrargyri Nigra contains mercurous oxide and is prepared by treating the insoluble mercurous chloride with lime water.

Lead.—Most of the lead salts are insoluble, and solutions of lead acetate and lead subacetate, the most commonly used salts of this metal, give a precipitate with the soluble hydroxides, carbonates, sulphates, sulphides, chlorides, bromides, iodides, phosphates, citrates, tartrates, benzoates, salicylates, tannates and any organic substance containing tannin. In certain hair lotions lead sulphide is the desired ingredient, and lead acetate and sulphur are purposely combined. Mucilage of acacia is also incompatible with the lead salts.

Zinc and Copper.—Solutions of zinc and copper salts give a precipitate with the alkaline hydroxides, carbonates, phosphates and borax.

Silver.—Silver nitrate is incompatible with the metallic chlorides and the hydrochlorides of the alkaloids, silver chloride being insoluble. Distilled water must be used for silver solutions.

2. The Decomposition of Carbonates, Bicarbonates and all Alkaline Preparations by Acid Preparations.

Examples.—The carbonates and bicarbonates of sodium, potassium and ammonium, aromatic spirit of ammonia and other alkaline preparations are decomposed by all the acids except hydrocyanic acid, and by the following acid preparations: Caffeine citrate, syrup of lemon, syrup of squill, vinegar of squill, oxymel of squill, vinegar of ipecacuanha and glycerin of pepsin. Chalk mixture contains calcium carbonate, and must not be prescribed with diluted or aromatic sulphuric acid. Liquor Bismuthi et Ammonii Citratis is incompatible with all the diluted mineral acids.

Bismuth oxynitrate or bismuth salicylate and a bicarbonate react together, with the production of carbon dioxide sometimes in sufficient quantity to burst the bottle. Bismuth oxycarbonate should be prescribed when an alkaline carbonate or bicarbonate is to be added.

When borax is mixed with glycerin, as in Glycerinum Boracis, free boric acid is formed, and bicarbonates cannot, therefore, be prescribed with the mixture. The evolution of carbon dioxide is sometimes sufficient to burst the bottle. Hydrocyanic acid does not decompose the alkaline bicarbonates, but it should not be prescribed with the alkalies. Linimentum Terebinthinæ Aceticum must not be prescribed with Linimentum Ammoniæ or with Linimentum Camphoræ Ammoniatum.

3. The Decomposition of the Salts of certain weak Organic Acids by means of a Mineral Acid.

Examples.—Benzoic acid, salicylic acid and cinnamic acid are very sparingly soluble, hence the benzoates, salicylates and cinnamates of sodium, potassium and ammonium are incompatible with caffeine citrate, acid infusion of roses, syrup of lemon and all acids, with the exception of acetic, boric and hydrocyanic acids.

4. The Decomposition of Iodides resulting in the Production of Free Iodine.

Examples.—An aqueous solution of potassium, sodium, ammonium or calcium iodide is decomposed by diluted nitro-hydrochloric acid, diluted nitric acid and the solution and tincture of ferric chloride, with a liberation of iodine. Iron and ammonium citrate and iron and potassium tartrate are compatible with the iodides.

Spirit of nitrous ether and nitrites in acid solution liberate iodine from iodides, and give off oxides of nitrogen, but in alkaline solution the combination is compatible. Spirit of nitrous ether becomes acid on keeping, and should always be neutralised when mixed with iodides.

Potassium chlorate mixed with syrup of ferrous iodide is gradually reduced to potassium chloride, and free iodine is liberated.

5. The Precipitation of Alkaloids from Solutions of their Salts and other Liquid Preparations containing them.—In view of the highly poisonous character of many of the alkaloids, their incompatibilities are of great practical importance.

Examples.—The various alkaloidal precipitants may be grouped in the following classes—

(*a*) Caustic alkalies, ammoniacal tinctures and other preparations containing ammonia, and alkaline carbonates, bicarbonates and borax. Nearly all the alkaloids in the free state are very sparingly soluble in water, but most of their salts are soluble in water. It may be stated as a general rule, that all salts and solutions alkaline to litmus precipitate the sparingly soluble free alkaloid from a solution of an alkaloidal salt, unless a large excess of water is present.

Solution of strychnine hydrochloride is very frequently prescribed with bicarbonates or with aromatic spirit of ammonia, and such a mixture is perfectly safe if care be taken to prescribe a quantity of the vehicle sufficient to keep the liberated strychnine alkaloid in solution.

The solubility of strychnine in water is approximately 1 in 7000, and from this figure it follows that one fluid ounce of water is required to dissolve the strychnine liberated from six minims of Liquor Strychninæ Hydrochloridi; by the addition of the alkali with a smaller quantity of the vehicle the strychnine would crystallise out on the sides of the bottle. Liquor Arsenici Hydrochloricus is acid, and

should be chosen to combine with alkaloids in preference to Liquor Arsenicalis, which is an alkaline solution of arsenic.

(*b*) The iodides, bromides, salicylates and benzoates of all the commoner alkaloids are notably insoluble in water. Avoid these salts in combination with Ferri et Quininæ Citras and Quininæ Sulphas.

If iodides or bromides are prescribed with solution of strychnine hydrochloride, precipitation may not take place immediately, and hence proper suspension of the precipitate is not ensured, and in consequence it is possible that the last dose in the bottle may contain a dangerous quantity of the insoluble alkaloidal salt. Donovan's solution—Liquor Arsenii et Hydrargyri Iodidi—is a particularly notorious alkaloidal precipitant, and should never be prescribed with alkaloids.

(*c*) Tannic acid, which is present in most of the vegetable infusions and decoctions, precipitates as tannates nearly all alkaloids from aqueous solutions. Infusion of quassia and infusion of calumba contain no tannin; all the other vegetable infusions will precipitate quinine tannate from a quinine solution. Gallic acid does not precipitate alkaloids.

(*d*) Mercuric chloride precipitates nearly all the alkaloidal salts from aqueous solution, and the combination of Liquor Hydrargyri Perchloridi with Liquor Strychninæ Hydrochloridi should be carefully avoided.

6. The Decomposition of Glucosides by Hydrolysis when mixed with Mineral Acids and Alkalies.

Examples.—Glucosides are decomposed by prolonged contact with mineral acids and alkalies. Salicin is slowly changed to saligenin and glucose, and the strophanthin in tincture of strophanthus is slowly decomposed even in neutral mixtures.

7. The Decomposition of Substances rich in Oxygen by means of readily Oxidisable Substances.

Examples.—Chlorates, nitrates, bichromates and permanganates rubbed in a mortar with oxidisable substances, such as charcoal, sulphur, reduced iron, sugar, hypophosphites, tannic acid, camphor or essential oils, are decomposed, sometimes with explosive violence.

Silver nitrate, silver oxide and potassium permanganate made into pills with the ordinary pill excipients are decomposed. A mixture of kaolin with hard and soft paraffin should be used.

A solution of potassium permanganate is reduced by ferrous salts, glycerin, alcohol, solution of hydrogen peroxide, carbolic acid and most organic substances.

8. The Decomposition of Chloral Hydrate by Alkalies and Alkaline Carbonates. The Formation of Chloral Alcoholate in the presence of Alcohol and a Soluble Salt.

Examples.—An aqueous solution of chloral hydrate is decomposed by the hydroxides and carbonates of sodium, potassium and ammonium, and by borax, with the production of chloroform and a formate of the base.

When chloral hydrate in aqueous solution is mixed with alcohol in the presence of certain soluble salts, such as potassium or sodium bromide, an oily-like layer of chloral alcoholate separates out.

9. The Formation of a Deeply Coloured Solution resulting from the Interaction of two Colourless or Nearly Colourless Solutions.—This class of incompatible compounds is relatively unimportant, and the combinations are for the most part therapeutically harmless.

Examples.—Infusions, decoctions, tinctures, and other liquid preparations containing tannic and gallic acid, produce bluish-black unsightly mixtures with iron salts, due to the formation of iron tannate. With the exception of quassia wood, calumba root and chiretta, all vegetable drugs contain more or less tannic acid.

Ferric chloride and other ferric salts with salicylates, give a deep purple colour from the formation of ferric salicylate.

Ferric chloride with acetates produces a dark red colour from the formation of ferric acetate, and with carbolic acid a bluish-violet colour due to the formation of ferric carbolate.

Phenazone and spirit of nitrous ether give a bright green colour, due to the production of a nitroso derivative of phenazone.

Sodium salicylate and spirit of nitrous ether give a reddish-brown colour sooner or later.

Physical Incompatibility

Under this heading may be emphasised the necessity for prescribing a sufficient quantity of solvent to dissolve completely any soluble salt, in doubtful cases a table of solubilities should be consulted. One part of pure phenol is soluble in twelve parts of water at 15° C., with less water a layer of liquid phenol will form and may be dangerous if unobserved.

The following examples are of more interest to the dispenser than to the prescriber; they are not dangerous to the patient, and if due precautions be taken, an unsightly mixture need not result.

1. The Combination of Fixed and Essential Oils, Resins and Similar Substances with Aqueous Liquids.

Examples.—All fixed and essential oils can be rendered miscible with water by emulsification with gum acacia.

Solid resins can be exhibited in mixture form by suspension in a finely powdered state with mucilage of tragacanth.

Resinous tinctures such as tincture of asafetida, compound tincture of benzoin,

tincture of Indian hemp, ammoniated tincture of guaiacum, tincture of myrrh and tincture of tolu, and resinous liquid extracts, such as liquid extract of male fern, give a precipitate of resin when added to water. This resin can be suspended in a finely divided state by the addition of mucilage of acacia to the mixture in the proportion of one part of mucilage for every seven parts of water to be added. Ammoniated tincture of quinine gives a precipitate of quinine hydrate when diluted with water, and should be treated in a similar way.

2. The Separation of Salts from a Solution resulting from the Addition of Liquids in which they are Insoluble.

Example.—A tincture strong in alcohol, such as tincture of ginger, may cause the partial separation of magnesium sulphate from a strong aqueous solution, magnesium sulphate being insoluble in alcohol. The obvious way to overcome this difficulty is to prescribe so much water that there is no danger of the solution crystallising.

3. The Decomposition of Two Substances, which, mixed in a Powdered Condition, form a more or less Liquid Mass.

Examples.—Mixtures of sodium sulphate and potassium citrate, zinc sulphate or alum with acetate of lead, potassium nitrate and sodium citrate, produce a semi-liquid mass, owing to the liberation of water of crystallisation.

Phenazone and sodium salicylate liquefy when mixed together, owing to the formation of phenazone salicylate.

Mixtures of camphor and chloral hydrate, camphor and menthol, and camphor with phenol, also form a syrupy liquid, and are often intentionally prescribed together.

R. R. B.

ACIDS AND ALKALIES

Of the fifty acids named in the Pharmacopœia, comparatively few hold their place by virtue of their acidity. Hydrocyanic, arsenious, salicylic and many other acids are of importance on account of properties, generally shared by their salts, which are quite independent of their feeble acidity.

The strong mineral acids, such as sulphuric, nitric and hydrochloric, have a corrosive action when applied in concentrated form to the tissues. The same is true of the caustic alkalies. All these substances have been used in the treatment of warts and other cutaneous thickenings. The most satisfactory and that generally used for such purposes is nitric acid. Its advantage lies in the fact that it does not dissolve the protein material which it has altered, and therefore its action is much better localised than that of sulphuric acid which chars or caustic potash which dissolves the skin. As milder caustics, for application to growths in the mouth and pharnyx, strong solutions of weaker acids, such as lactic and phosphoric, have been used.

A most important property of the caustic alkalies, including potash, soda and ammonia, is their power of dissolving fat and oil to form soluble soaps. Owing to this they are of great value as cleansing agents. This property is shared by the salts of weak acids with strong bases, such as the carbonates of sodium and potassium; the alkalinity of such solutions depends on their hydrolytic dissociation.

In the description of any aqueous solution one of the first points claiming the attention of the bio-chemist is whether the solution is acid, alkaline or neutral. All living processes go on in aqueous solutions or in tissues bathed in and permeated by such solutions. So also the extra-cellular processes of digestion are conducted in aqueous solution; it is shown experimentally that the course of intra- and extra-cellular processes is intimately dependent on the reaction of the solutions present.

In the action of the gastric juice it has long been recognised that titration with alkali does not give sufficient information as to the acidity of the digestion mixture. Solutions of pepsin acidified on the one hand with lactic or acetic acids and on the other hand with hydrochloric or nitric acid possess very different digestive activities, even though they all require equal quantities of soda to make them neutral to litmus. The difference does not depend upon any poisonous action of the lactic or acetic acids, but on the fact that the reaction of such solutions is *not so acid* as that of the solutions of mineral acids.

The physico-chemical conception of *reaction* is of fundamental importance in many branches of physiology and pharmacology.

Pure water and all aqueous solutions contain hydrogen ions and hydroxyl ions. In pure water a very small proportion of the H_2O molecules are split into the ions $H^{\cdot}$ and OH'. The proportion thus split depends on the temperature: it may be measured by conductivity determinations. The electrical conductivity of pure water is very slight: in a litre of water at room temperature only 10^{-14} gram molecules of water are ionised. Since each molecule of water yields one hydrogen and one hydroxyl ion the numbers of $H^{\cdot}$ and of OH' ions in the water is the same. Neutrality signifies the equality of hydrogen and hydroxyl ion concentration.

If to pure water is added some substance which dissociates yielding hydrogen ions in greater concentration than they are present in water (as, for example, hydrochloric or acetic

acid), or some substance which dissociates to yield an ion with a great affinity for hydroxyl ions (as, for instance, ferric chloride), the hydrogen ion concentration is increased and the hydroxyl ion concentration diminished; the solution becomes acid. Conversely, if a substance is added to water which yields any considerable amount of hydroxyl ions (such as caustic soda or ammonium hydroxide), or which yields ions with a great affinity for hydrogen ions (as, for instance, sodium carbonate or borax), the hydrogen ion concentration is diminished and the hydroxyl ion concentration increased; the solution becomes alkaline. In any aqueous solution at a given temperature the product of the concentrations of hydrogen and hydroxyl ions is constant: thus if either the hydrogen or hydroxyl ion concentration is measured both are known. At room temperature a solution containing 10^{-7} gram ions per litre of hydrogen ions is neutral; one containing more than this concentration is acid, one containing less than this concentration is alkaline.

Now the hydrogen ion concentration of water is so low that a very small addition of hydrogen ions will greatly alter it. Thus a single drop of normal hydrochloric acid would suffice to increase the hydrogen ion concentration of some fifty litres of water ten times. The same low stability of reaction characterises pure solutions of neutral salts of strong acids and strong bases. Such substances as sodium or potassium chloride will not appreciably alter the hydrogen ion concentration of solutions to which they are added. Quite otherwise is it when the salts of weak acids or bases are concerned. It is familiar to every one that a solution of sodium carbonate is distinctly alkaline. Similarly a solution of aluminium or of zinc chloride in water is distinctly acid. The effects of such substances on the reaction of the water depends always on the affinity of one or the other of the ions into which the dissolved substances dissociate for one of the ions into which water dissociates. When an aqueous solution contains substances of this kind, or amphoteric substances like the amino-acids or their compounds the proteins, the addition of acid or of alkali produces much less effect on the reaction of the solution than is produced by their addition to plain water. The stability of the hydrogen ion concentration of the solution is increased—because it now depends on more than one equilibrium. Such materials as tend to stabilise the reaction of a solution have been called by Sörensen "buffers." Different combinations of "buffers" may stabilise the reaction of a solution in different regions. Thus a mixture containing boric acid and soda may be changed but little in reaction, even during considerable additions of acid and alkali.

The hydrogen ion concentration of a solution is found by measuring the potential difference between the solution and a plate of platinum coated with platinum black, immersed in the solution and saturated with hydrogen gas. At a given temperature the relation between this potential difference and the logarithm of the hydrogen ion concentration is accurately known. Another method, which can be carried out very simply in those cases where it is applicable depends on the fact that standard "buffer" solutions of known hydrogen ion concentration can be prepared. The hydrogen ion concentration of an unknown solution may be compared with a series of such standard solution by the use of certain indicators. The method has been applied to the study of urine.

For discussion of the whole question reference should be made to the admirable work of Sörensen and his school, to whom the recent development of the subject is in great measure due (cf. Sörensen, *Ergebnisse d. Physiol.*, 1912.)

Action of Acids and Alkalies in the Alimentary Tract

Alteration in the reaction of the contents of the alimentary canal by taking acid or alkaline solutions by the mouth may affect the digestive processes in two distinct ways, by modifying the amount of secretion from certain glands, and by altering the rate of progress of the enzyme actions which constitute digestion.

In the Mouth.—Acid solutions produce an effect dependent chiefly on their hydrogen ion concentration. It is easy to recognise in such a series as this: boric, carbonic, lactic and hydrochloric acids in dilute equivalent solutions, an increasing degree of sourness with the increasing amount of dissociation. Too highly acid a solution is painfully astringent and may damage the teeth by dissolving their calcium salts. Acids cause a reflex secretion of saliva, and upon this fact depends the value of such preparations as lemonade or lime-juice in quenching thirst, especially in fevers.

The activity of ptyalin is most rapid in a solution very near the neutral point. It is inhibited by excess of acid or alkali. It is evident, therefore, that if acids are used to increase the secretion of saliva, they should not be mixed with starchy food, but should precede its ingestion. The actual digestion of starch goes on chiefly in the stomach in the interior of a bolus before it is penetrated by the acid gastric juice.

In the Stomach.—The action of pepsin can proceed only in solutions of sufficiently great hydrogen ion concentration. The optimum

hydrogen ion concentration for the action of pepsin is about 10^{-2} gram ions per litre. This is the reaction possessed by a centi-normal solution of hydrochloric acid.

In the stomach, where there is much lactic or butyric fermentation, the titration acidity to alkali may be higher than normal, yet the hydrogen ion concentration of the digesting mass may be too low and the digestion, for this reason, imperfect. The administration of hydrochloric or nitric acids in suitable dilution is required to render the gastric juice of sufficient hydrogen ion concentration for digestion to proceed normally. The increased hydrogen ion concentration will also inhibit the progress of bacterial fermentation. Given before a meal, hydrochloric or nitric acid is said to diminish the quantity of gastric juice secreted: after a meal it aids the digestion of protein matter in the stomach. The time of administration is therefore of great importance. Alkaline substances, such as sodium carbonate, are often given to correct excessive acidity in the stomach where this is due to hypersecretion of gastric juice. The doses given, and found empirically to be beneficial, are far too small to produce any appreciable neutralisation of the quantities of acid secreted under ordinary circumstances. According to the work of Pawlow they act by reducing the amount of secretion of gastric juice.

In the Intestine.—The passage of the gastric contents into the duodenum produces two important results through the acidity of the chyme. A reflex closure of the pylorus is brought about, and the liberation of secretin by the action of the acid on the pro-secretin contained in the mucosa is responsible for stimulation of the pancreas. The secretin is carried in the blood to the pancreas, which it rouses to activity. Too slight acidity of the gastric contents may thus interfere not only with digestion in the stomach but also in the intestine. In the duodenum the chyme is rendered alkaline by the pancreatic juice, the bile and the succus entericus. The activity of trypsin (an enzyme formed by the action of enterokinase on trypsinogen, a precursor contained in the pancreatic juice) is exerted only in distinctly alkaline solution.

Moreover, the pancreatic lipase can act only in alkaline solution: the digestion of fat depends further on the immediate formation of soaps from the fatty acids liberated. Since the reaction of the duodenal contents depends on the neutralisation of the chyme by the alkali of the intestine it is evident that the titration acidity of the stomach contents will have to be taken into account in this connection. A stomach containing large quantities of feebly dissociated acids, the products of bacterial fermentation, may have too low a hydrogen ion concentration for peptic digestion to proceed properly and yet may have a titration acidity so great that it is imperfectly neutralised, or at any rate made insufficiently alkaline in the intestine for the adequate action of trypsin and of lipase. It thus appears that the administration of hydrochloric acid may in some cases be the best way of increasing the alkalinity of the small intestine.

Reaction of the Blood and Tissues

The reaction of the blood and tissues is normally slightly on the alkaline side of the neutral point. The hydrogen ion concentration of the blood is about 10^{-8}, the same as that of sea-water, and the reaction is stabilised by the presence of the same buffers as those in the sea-water, carbonates and phosphates. In addition there are present proteins which by their amphoteric property assist in limiting changes in the reaction of the blood. In contrast with the gross changes in reaction which occur in different parts of the gut, the reaction of the blood changes but very slightly during life. Yet the small changes which occur are possibly of great importance in the co-ordination of functions in the body. The regulation of the reaction of the blood depends on a variety of factors. These include the separation from the blood of the acid and alkaline digestive secretions, the function of the kidneys in pouring out a more or less acid urine, and especially on the elimination of carbon dioxide by the lungs. The carbon dioxide in the alveolar air is in equilibrium with dissolved carbonic acid in the blood, which is in turn in equilibrium with carbonates and thus related to the whole complex of equilibria in the blood in which the hydrogen and hydroxyl ions take part.

Small changes in the reaction of the blood modify the behaviour of the respiratory centre, the vasomotor centre and the heart. Thus in acapnia, where by excessive ventilation of the lungs the carbon dioxide is largely washed out of the blood, the automatic activity of the respiratory centre is upset (apnœa), the blood pressure drops, and the output of the heart is reduced because its relaxation becomes imperfect.

Similar effects are produced by the injection of fairly large doses of alkali. On the other hand, if the reaction of the blood is rendered more acid, as by partial asphyxia, there is greatly increased activity of the respiratory centre, the blood pressure rises, the heart becomes dilated and its contractions less complete. It is noteworthy that the effects produced on the heart by asphyxiation, such as heart-block and diastolic arrest, can also be produced by perfusing

the isolated organ with solutions of higher concentration in hydrogen ions than normal. The influence of changed reaction on the behaviour of living tissues is specially interesting because by their own activity the tissues alter their own reaction, and it is in fact here that we find the link between activity and its after-effects. Not only are the final products of metabolism in muscle acid (carbonic acid), but an intermediate stage in metabolism is known to involve the formation of a stronger acid than carbonic, namely, lactic acid. Subsequently the lactic acid is removed by oxidation, and thus it comes about that when oxidation is interfered with by reduction in the oxygen supply, the tissues and the blood become less alkaline. Incomplete oxidation of fat, as well as of carbohydrate, leads to an excess of acid substances, and it is now generally recognised that the condition of acidosis, where acid substances, in particular aceto-acetic and β-oxy-butyric acids, are found in the urine is the result of the incomplete oxidation of fat.

The injection of alkaline solutions, such as sodium carbonate or bicarbonate, has a most beneficial, though transient, effect in such conditions and especially in diabetic coma. It is found also that sodium citrate is particularly effective.

The recent work of Barcroft and his pupils shows that slight changes in the reaction of the blood have an important effect on the affinity of hæmoglobin for oxygen, and that such changes influence the passage of oxygen from blood to tissues.

Increased hydrogen ion concentration in the tissues has an important effect in disturbing their relations to water. Treated with faintly acid solutions such tissues as muscle, liver or kidney swell very markedly in isotonic saline solutions. There is good reason for believing that acidification is a common cause of œdema. Œdema can be produced by interference with the blood supply to a limb for example, and its occurrence depends on the relatively acid condition produced in the absence of complete oxidation. It has been found that the effects of swelling due to acid can be averted not only by treatment with alkali, but even better by the use of certain salts with polyvalent acid radicles. The citrate of sodium is peculiarly effective. Excellent results in various localised œdemas have been reported as a result of injecting solutions of this salt. It has proved of value in the treatment of glaucoma.—(M. Fischer.)

It has been shown by Fletcher and Hopkins that there is a considerable liberation of acid in muscle on injury. It is very probable that the swelling consequent on a bruise is to be explained as a local œdema due to the local acidity.

The mechanisms for regulating the ionic concentration of the blood are so perfect that it is not easy to produce any considerable change by administering acids or alkalies in the food. Yet it is possible to alter the reaction of the urine to a considerable extent. The administration of mineral acids such as sulphuric or phosphoric causes a slight increase in the acidity of the urine and a diminution in the urea output. This does not signify any decrease in the nitrogenous metabolism, but only that a larger proportion of the nitrogen is excreted in the form of ammonia. Organic acids such as citric and tartaric are to some extent absorbed and oxidised to carbonates. They may actually render the urine more alkaline.

The carbonates of potassium or lithium administered by the mouth render the urine alkaline: they are employed to prevent the deposition of uric acid in the tissues. It must, however, always be borne in mind that the effects of the administration of acids or alkalies on the activity of the digestive glands must have an important influence on their general action. G. R. M.

ACIDS: PHARMACOLOGY AND THERAPEUTICS

Dilute acids mainly exert their actions from their power of neutralising alkalies, and as most living tissues exist in an alkaline medium, the neutralisation of this leads to death of the tissues. Thus acids must be considered as protoplasmic poisons, and, as such, they are all antiseptics to a certain degree although too irritant for most ordinary purposes. This disinfectant action depends on the dissociation of the H ions, although certain organic acids —formic, acetic, boric—disinfect more powerfully than the H dissociation would imply, owing to the fact that, being lipoid-soluble, they can penetrate more easily.

External Actions.—Most strong acids if applied to the skin act as *caustics* by causing destruction of the epidermis through their power of precipitating proteins, extracting water from the tissues, and neutralising the alkalinity of the cells; in the case of powerful mineral acids the process is painful and, if the area affected be large, as in acid throwing, severe collapse may ensue. When used to destroy surface growths they do not penetrate so deeply as alkalies, since the alkaline reaction of the subcutaneous tissues helps to neutralise them. Sulphuric acid not only destroys the tissues, but also chars them, and a black pellicle results which on falling off leaves a scar. Hydrochloric acid is more useful than sulphuric, although on ac-

count of its volatility it tends to spread on penetrating the subcutaneous tissues. Nitric acid stains the skin yellow, but seldom leaves permanent scars; the fact that it does not redissolve the precipitated proteins limits its penetrative powers. Glacial acetic and lactic acids are less powerful but efficient caustics. Carbonic acid snow is used as a cure by freezing of nævi, lupus, warts, rodent ulcers, etc. Acids are principally employed as caustics for external epithelial growths of a benign nature. Weaker solutions of acids act as rubefacients or vesicants, and on raw surfaces they are irritant and astringent.

Dilute solutions of acids applied to the skin are *refrigerants* and lower the temperature in fever; this is attained largely by their evaporation, but certain of them are said to exert a definite astringent action and to check sweat secretion. They may be applied to the surface of the skin in dilute solution by sponging. Most commonly employed are acetic acid, citric acid, and sulphuric acid in febrile conditions, local perspiration, and to diminish the sweating of phthisis. Lotions containing dilute nitric acid are occasionally of value in itching skin affections.

Dilute nitro-hydrochloric acid has been administered in the form of baths for the treatment of chronic liver complaints and the application of folds of flannel soaked in the acid (2–3 fl. dr. to 1 pint) over the hepatic region has been found useful. The method was brought into use by Scott of Bombay and used with success in India by Annesley and Martin. Martin's method consisted in mixing 3 oz. hydrochloric acid, and 2 oz. nitric acid with 5 oz. water; 6 oz. of this mixture in two gallons of water form a bath, which may be heated by the addition of warm water if necessary. Naturally the bath must be of porcelain or wood. The whole body may be immersed in the bath, but generally a foot-bath is used. It should last 10–15 mins. and be repeated twice daily.

Baths of carbonic acid in effervescing form have a distinct stimulant action on the surface of the skin and promote dilation of the peripheral vessels. The heart's action is relieved and strengthened and the blood-pressure falls. In the Schott-Nauheim treatment of heart-disease such baths are largely employed, the water employed containing at the same time sodium and calcium chlorides (*see* Sod. Bicarb.).

Internal Actions. *Mouth.*—Acids reflexly augment the salivary secretion, principally that of the submaxillary gland, and stimulate appetite. At the same time they exert a slight astringent effect in the mouth and throat by precipitating the albumin in the superficial layers of the mucous membrane. Since they are liable to affect the teeth, it is advisable that they should be taken through a tube. Acid fluids act as internal refrigerants, satisfying the thirst of febrile conditions; this is a direct result of the increased secretion of saliva which keeps the mouth moist; those employed for this purpose are dilute solutions of citric (lemon juice), tartaric, acetic and effervescing carbonic acids.

Stomach.—Opinions have differed as to the action of acids on the secretion of gastric juice. Acids administered previous to meals were believed to inhibit gastric secretion although Pawlow thought the reverse was the case. The question is by no means settled, and with fairness it may be asserted that in all ordinary cases acids have little influence on the secretion of gastric juice. Acids directly augment the acidity of the gastric juice, but Boldyreff has shown recently that there is a self-regulation of the acidity of the stomach contents. Fresh gastric juice contains 0·5 per cent. HCl, but this is rapidly lowered in the organ to about 0·2 per cent. HCl. If any foreign acids are introduced this levelling or diluting effect is also accomplished, while neutral, alkaline or feebly acid fluids provoke a secretion of acid to bring the concentration up to normal. Excess of acid is neutralised by a reflux from the contents of the duodenum. Where achlorhydria exists, as in chronic gastric catarrh and carcinoma, the addition of acid is necessary, as it is essential to the action of pepsin; in such cases hydrochloric acid should be selected for obvious reasons. It is administered in dilute form from half-an-hour to an hour after meals. Prolonged administration of acids is inadvisable as it may give rise to gastric catarrh. While acids applied to isolated stomach muscle diminish its tone, they have little effect on the movements of that organ when administered internally. Carbonic acid, however, stimulates peristalsis of the stomach, and its administration in effervescing form thus becomes of value in atonic conditions.

Acids play a very important part in the opening and closure of the pylorus. A slight acidity on the stomach side of the pyloric ring forms the stimulus which relaxes the pyloric tone and allows the stomach contents to pass into the duodenum. Acidity on the duodenal side of the pylorus produces closure of the pyloric valve. It is obvious, therefore, that both diminished and excessive acidity of the stomach contents will cause pyloric spasm with consequent stasis of the food.

Intestine.—On reaching the duodenum, acids perform the important function of indirectly stimulating the flow of pancreatic juice (*vide supra*). They are at the same time neutralised. Certain acids, and more particularly nitro-

hydrochloric acid, are believed to augment the biliary secretion and to act as cholagogues; while there is little experimental confirmation of this assertion, it is nevertheless clinical experience that nitro-hydrochloric acid is a useful remedy in congestion of the liver, biliary dyspepsia, and hepatic torpidity. The secretion of the intestinal glands is diminished by acids; they exert also a slight astringent action, this being most marked in the case of sulphuric acid, which is occasionally employed in treating diarrhœa.

Remote Effects following Absorption.—Acids after being absorbed render the blood plasma less alkaline by combining with some of its basic constituents; they cannot, however, render it acid. Herbivorous animals are much more sensitive to acids than carnivora, for the latter can neutralise the excessive acid by ammonia, which power the herbivorous animals do not possess, hence in them the acid combines with the essential sodium and potassium bases to the detriment of the organism. In carnivora there is increased excretion of ammonia in the urine pointing to either increased protein metabolism or to a combination of acid and ammonia preventing the latter's conversion into urea.

Since acids diminish the alkalinity of the tissues it would be anticipated that they would influence metabolic functions. Diminished alkalinity of the blood plasma leads to increased autolysis or destructive metabolism of proteins, and there is less production of CO_2 and diminished intake of O with, as a result, increased lactic acid formation and possibly fatty degeneration. The tonic effects of acids must be ascribed to their powers of improving digestion and metabolism. Hydrochloric acid and nitrohydrochloric acid are said to increase the number of red corpuscles but not the hæmoglobin.

By forming salts in the tissues, they act ultimately as saline diuretics increasing the excretion of urine, but they do not as a rule increase its acidity to any marked degree; in fact, nitric acid by a process of decomposition to ammonia may actually diminish it. Acids have been given in oxaluria with benefit, but their action in this connection is uncertain.

Other Actions of Acids.—Solutions of acids diminish the tone of skeletal, unstriated and heart muscle. If the frog's heart be perfused with acids, a gradual weakening of the systole occurs and ultimately the heart stops in diastole. Perfusion of the mammalian heart with hydrochloric acid causes dilatation of the coronary arteries. Intravenous injections of acids lead to increased cardiac action associated with dyspnœic respiration, but with large doses a deleterious influence is exerted on the nervous centres, the vaso-motor, respiratory and cardiac centres being paralysed. Added to blood, acids coagulate the albumin and form acid methæmoglobin, or acid hæmatin according to their strength. Conc. sulphuric acid decomposes hæmoglobin to acid hæmatoporphyrin. Acids, more especially acetic acid, are occasionally employed in obesity; the method is not to be encouraged as the diminution in weight is caused chiefly by the induction of gastro-intestinal catarrh.

Toxicology. *External.*—Corrosive acids may occur as toxic agents from external application as the result of "acid-throwing." The most commonly employed is sulphuric acid (vitriol-throwing) and the part affected is usually the face. The integument in such cases is corroded in patches and stained white or faintly yellow if hydrochloric acid be the causative agent, deep yellow if nitric acid has been employed, and charred by sulphuric acid. Except where carbolic acid has been the cause, these corroded areas are intensely painful and, should they be large, shock and severe collapse are secondary results. Where the acid has reached the eye the condition is to be regarded seriously, loss of sight frequently occurs, and enucleation may be necessary.

Internal.—The symptoms of poisoning by strong acids when taken internally are those of corrosion. There are marks of superficial erosions on the lips and at the angles of the mouth, the mucous membrane of the mouth and throat are excoriated, inflamed, intensely painful, and coated with a pellicle stained according to the acid employed. Where hydrochloric or nitric acid has been employed the irritant vapours evolved may cause spasm of the glottis and swelling of the larynx with consequent rapid death from suffocation. If the acid has been swallowed there is severe pain in the stomach, followed by vomiting; the person becomes collapsed, the pulse feeble and quick, while respiration is shallow. On swallowing the acid the symptoms set in immediately with violent burning pain extending from the mouth to the stomach, gastric eructations and attempts at vomiting. The vomit is black or brownish, containing portions of exfoliated mucous membrane and coffee-ground sediment. These vomiting acts are attended with great pain, as are also attempts at swallowing in order to relieve the intense thirst. The constant retching leads to collapse, diarrhœa may occur, the pulse becomes rapid and feeble, respiration weaker and a cold sweat breaks out. The mental faculties usually remain clear till late, and death occurs from convulsions, suffocation, exhaustion, or sudden collapse following perforation of the stomach. Even when cases recover from the primary poisoning death may

occur late from stricture of the œsophagus or larynx.

Post-mortem.—The tissues from the mouth to the stomach are stained brown, white or yellow and excoriated, softened and very friable; the œsophagus is usually corroded in patches. The stomach contents in the case of sulphuric acid are dark brown and have the appearance of charring; with nitric acid the contents are yellow; the mucous membrane is corrugated, excoriated, and may or may not be perforated.

Treatment. *External.*—The acid should be washed off with soap and water, or with water containing washing soda or bicarbonate of soda, which by effervescence indicate the presence of acid. After neutralisation of the acid, treat as burns. If the eye be affected, wash out with water containing a little salt and bicarbonate of soda. After neutralisation apply cocaine and a little olive oil inside the lids.

Internal.—(1) Avoid using the stomach pump, it may precipitate perforation. (2) Administer alkalies such as soft soap and water, lime water, magnesia or weak solutions of sodium or potassium hydrate. Scrapings of whitewash from the walls of a room are useful in urgent cases. Washing soda and sodium bicarbonate may be employed, although they are to be avoided if perforation is anticipated, since CO_2 is evolved. (3) Administer large quantities of demulcents in water—white of egg, milk, gruel, etc. (4) Morphine hypodermically to ease the pain and obviate collapse.

Acidum Sulphuricum (B.P.). H_2SO_4. Characters, colourless, oily, intensely acid liquid. Sp. gr. 1·841, contains 95 per cent. of real acid; gives white ppt. with barium chloride.

(*a*) Acidum Sulphuricum Dilutum (B.P.). Contains 10 per cent. of acid.
Dose : 3–12 dl. (5–20 min.).

(*b*) Acidum Sulphuricum Aromaticum (B.P.). Contains 7 per cent. of acid with tincture of ginger, spirit of cinnamon and alcohol.
Dose : 3–12 dl. (5–20 min.).

(*c*) Acidum Sulphuricum Alcoholisatum. Sulphuric acid 1; alcohol 3, forms sulphovinic acid.
Dose : 1–6 dl. (2–10 min.).

(*d*) Mistura Acidi Sulphurici cum Opio. Contains dilute sulphuric acid, tincture of opium and tincture of capsicum.
Dose : 15–30 ml. (½–1 fl. oz.).

Special Therapeutics.—It is employed as an astringent for bleeding surfaces, the acidum sulphuricum alcoholisatum, well diluted, forms a useful refrigerant and checks perspiration. Sulphuric acid has a limited astringency in the intestine, and the aromatic acid is advised for cholera and diarrhœa. Internally it is an antidote to lead poisoning.

Acidum Hydrochloricum (B.P.). HCl. Characters, colourless, fuming, acid liquid. Sp. gr. 1·160; contains 31·79 per cent. of real acid. Gives a white ppt. with silver nitrate insol. in nitric acid.

(*a*) Acidum Hydrochloricum Dilutum (B.P.). Contains 10 per cent. of acid.
Dose : 3–12 dl. (5–20 min.).

Special Therapeutics.—It is most largely used in dyspepsia where there is deficiency of HCl in the stomach; and is often combined with pepsin. Occasionally it is employed as an astringent gargle.

Acidum Nitricum (B.P.). HNO_3. Characters, clear, colourless, fuming liquid. Sp. gr. 1·42; contains 70 per cent. of real acid.

(*a*) Acidum Nitricum Dilutum (B.P.). Contains 10 per cent. of acid.
Dose : 3–12 dl. (5–20 min.).

(*b*) Acidum Nitro-hydrochloricum. Aqua Regia. Contains nitric acid 1 part, hydrochloric acid 3 parts.

(*c*) Acidum Nitro-hydrochloricum Dilutum (B.P.). Contains nitric acid 12, hydrochloric acid 16, water 100 parts.
Dose : 3–12 dl. (5–20 min.).

(*d*) Balneum Acidum. Contains Acidum Nitro-hydrochloricum Dilutum 0·3, water to 100.

Special Therapeutics.—Nitric acid is the most commonly employed caustic for warts, nævi, moles, granulations, and indolent ulcers. It should be applied by a glass rod or match; repeated applications are best. The acid well diluted relieves itching of lichen and prurigo. Internally or in the form of a bath or compress, it and its preparations—especially nitro-hydrochloric acid—have been found useful in biliary congestion, dyspepsia and other liver complaints; they have, however, no specific cholagogue action on the liver.

Acidum Phosphoricum Concentratum (B.P.). H_3PO_4. Characters, syrupy, colourless liquid. Sp. gr. 1·5; contains 66.3 per cent. of real acid.

(*a*) Acidum Phosphoricum Dilutum. Contains 10 per cent of acid.
Dose : 3–12 dl. (5–20 min.).

(*b*) Mistura Acidi Phosphorici. 1 fl. oz. contains 15 min. dilute phosphoric acid, 10 min. emulsion of chloroform, and compound infusion of gentian.
Dose : 15–30 ml. ($\frac{1}{2}$–1 fl. oz.)

Special Therapeutics.—Phosphoric acid acts like mineral acids, but is less active. It is a useful refrigerant beverage in dilute form and remotely increases the acidity of the urine. It has none of the actions of phosphorus. It renders iron preparations compatible with astringent vegetable infusions.

Acidum Aceticum (B.P.). CH_3COOH. Characters, clear, colourless, pungent liquid. Sp. gr. 1·044; contains 33 per cent. of real acid.

(*a*) Acidum Aceticum Dilutum (B.P.). Contains 5 per cent. of acid.
Dose : 2–4 ml. ($\frac{1}{2}$–1 fl. dr.).
(*b*) Oxymel (B.P.). Contains acetic acid 10, water 10, honey 50.
Dose : 2–8 ml. ($\frac{1}{2}$–2 fl. dr.).
(*c*) Acetum, Vinegar. Contains 4–5 per cent. of acid.
Dose : 4–30 ml. (1–8 fl. dr.).
(*d*) Acetum Odoratum. Toilet vinegar. 1 of acetic acid in 8 of water with various aromatic principles.

Acidum Aceticum Glaciale (B.P.). Characters, clear, colourless liquid; crystallises below 14·7° C. Contains 98·9 per cent. of acid.

(*a*) Acidum Aceticum Aromaticum. Glacial acetic acid with odoriferous principles.

Special Therapeutics.—Acetic acid in dilute solution makes a good refrigerant, both externally and internally, for febrile conditions. In stronger concentration it is rubefacient. Acetum odoratum is a restorative, stimulating the nasal mucous membrane and reflexly the important medullary centres. The acid is mildly diaphoretic and diuretic. Glacial acetic acid is rubefacient, vesicant, and caustic. Owing to its volatility its action, however, tends to spread. It is employed for corns and warts.

Acidum Citricum (B.P.). $C_3H_4OH(COOH)_3$. Characters, it is obtained from several species of Citrus; colourless, prismatic, efflorescent crystals, soluble in water and alcohol; an 8 per cent. (35 gr. per oz.) solution is equivalent in strength to lemon juice. 20 gr. neutralise 28·5 gr. potassium bicarbonate, 24 gr. sodium bicarbonate, 15 gr. ammonium carbonate, and 14 gr. magnesium carbonate.
Dose : 3–12 dg. (5–20 gr.).

(*a*) Syrupus Acidi Citrici. Citric acid with syrup of lemon and syrup.

Acidum Tartaricum (B.P.). $(CHOH, COOH)_2$. Characters, colourless, translucent, monoclinic prisms; soluble in water and alcohol. 20 gr. neutralise 26½ gr. potassium bicarbonate, 22½ sodium bicarbonate, 14 gr. ammonium carbonate, 13 gr. magnesium carbonate.
Dose : 3–12 dg. (5–20 gr.).

Special Therapeutics.—Citric and tartaric acids are external and internal refrigerants, the former being more commonly employed. They are converted in the alimentary canal into alkaline citrates and tartrates, and act as mild saline purgatives. After absorption they are oxidised and excreted in the urine as carbonates, making the urine alkaline. Both acids are largely employed for the preparation of effervescing mixtures. It is doubtful whether citric acid diminishes the coagulability of the blood, and proof is wanting that in large doses it causes the shrinkage of thrombi, as has been asserted.

Acidum Sulphurosum (B.P.). H_2SO_3. Characters, colourless liquid, suffocating odour. Sp. gr. 1·025; contains 6·4 per cent. of acid.
Dose : 2–4 ml. ($\frac{1}{2}$–1 fl. dr.).

(*a*) Lotio Acidi Sulphurosi. Contains sulphurous acid with glycerine of tannic acid.
(*b*) Sodii Sulphis (B.P.). Na_2SO_3, $7H_2O$. Colourless efflorescent prisms.
Dose : 3–12 dg. (5–20 gr.).

Special Therapeutics.—Sulphurous acid is a powerful deoxidising agent and is by addition of oxygen converted into sulphuric acid; by removing oxygen from bacteria, etc., it acts as a disinfectant. The fumes of burning sulphur —in association with watery vapour—are a convenient way of using this acid as a room disinfectant; 3 lb. of sulphur should be allowed to 1000 cubic feet, and the room kept closed for twenty-four hours. Sulphur dioxide has the advantage of being a powerful insecticide, killing bugs, fleas, etc. Liquefied sulphurous acid is also supplied for disinfecting purposes, 15 oz. being sufficient for 1000 cubic feet. It is also of advantage as a local application in ringworm, scabies, and other skin diseases, while gargles are found useful in tonsillitis, and sprays in sore throat. Internally it has been given to arrest fermentative processes in the stomach due to sarcinæ, etc., and has proved useful in

cholera. It removes the stains of iodine and potassium permanganate.

Acidum Boricum (B.P.). H_3BO_3. Characters, colourless, odourless, shining scales, greasy to the touch; soluble in water 1 in 25.
Dose : 3–10 dg. (5–15 gr.).

(*a*) Glycerinum Acidi Borici (B.P.). 30 per cent. of acid in glycerin.
(*b*) Unguentum Acidi Borici (B.P.). 10 per cent.
(*c*) Collyrium Acidi Borici. 1 in 50.
(*d*) Lotio Acidi Borici. 1 in 30.
(*e*) Solvellæ Acidi Borici. 15 gr.

Borax Purificatus (B.P.). $Na_2B_4O_7$, $10H_2O$. Characters, colourless, efflorescent crystals or white powder, alkaline reaction, sweetish taste; soluble 1 in 25 of water.
Dose : 3–10 dg. (5–15 gr.).

(*a*) Glycerum Boracis (B.P.). 1 in 6 of glycerin.
(*b*) Mel Boracis (B.P.). 10 of borax in 5 of glycerin and 85 of clarified honey.
(*c*) Collyrium Boracis. 1 in 50.
(*d*) Gargarisma Boracis. 1 in 25.
(*e*) Trochisci Boracis. 3 gr. in each.
(*f*) Solvellæ Boracis et Cocainæ Compositæ. Borax 2 gr., cocaine hydrochloride $\frac{1}{10}$ gr., sodium chloride 6 gr., Boric acid 1 gr., benzoic acid $\frac{1}{4}$ gr., menthol $\frac{1}{100}$ gr., thymol $\frac{1}{100}$ gr.
(*g*) Unguentum Boracis. 1 in 8.

Special Therapeutics.—Boric acid is a mild antiseptic, causing no irritation; it is therefore useful as a surgical dressing; for this purpose boric acid lints and wool are provided for ophthalmic and aural practice, for burns and superficial wounds. Lotions and ointments are occasionally useful in skin diseases, where they relieve itching, while they are also useful in fœtid sweating. Mixed with starch, boric acid forms a dusting powder for infants. Solutions of borax and boric acid are useful as mouth washes for aphthæ and stomatitis, and as gargles or paints for tonsillitis and sore-throat. Internally solutions (1–3 per cent.) of boric acid are employed as disinfectants for the urinary passages, vagina and uterus and as disinfectant enemata. In gastric catarrh of infants the stomach may be washed out with boric acid solution. During excretion boric acid acidifies the urine and has mild disinfectant properties in the urinary tract. Large doses given internally cause gastro-intestinal irritation, and after absorption they possess a sedative action on the nervous system; borax has occasionally been of service in epilepsy, where bromides have failed.

Acidum Lacticum (B.P.). $CH_3CHOH.COOH$. Characters, syrupy, colourless, somewhat hygroscopic liquid. Sp. gr. 1·21. Contains 75 per cent. of acid.

(*a*) Syrupus Acidi Lactici. 1 in 40.
Dose : 4–8 ml. (1–2 fl. dr.).

Special Therapeutics.—Lactic acid is a product of muscular metabolism. It may be applied externally in diluted form in alopecia (1 in 3). It has been employed as a caustic in tubercular ulcerations of the pharynx and larynx, and as a spray in croup and diphtheria. In catarrhal conditions of the stomach, atonic dyspepsia, infantile and tropical diarrhœa, it is occasionally of service. Putrefactive disorders of the intestine are amenable to treatment with milk soured by the lactic acid bacillus (B. Caucasicum).

Acidum Chromicum (B.P.). CrO_3. Characters, deliquescent, dark-red needly-shaped crystals.

(*a*) Liquor Acidi Chromici (B.P). 25 % in water.
(*b*) Gargarisma Acidi Chromici. 1 in 500.
(*c*) Pigmentum Acidi Chromici. 10 gr. to 1 oz. of water.

Special Therapeutics.—Chromic acid is a powerful oxidising agent and acts as a disinfectant, deodorant and caustic. It has considerable powers of penetration, hence care must be taken—by guarding the surrounding tissues with soft paraffin—to limit its sphere of action. As a caustic the liquor may be used for warts, condylomata, granulations and indolent ulcers, etc. Solutions of 2–3 per cent. strength may be employed as antiseptics for hyperidrosis and for ulcers and papillomata of the mouth, pharynx and nose, particularly where these are of a syphilitic character.

Acidum Oxalicum. $(COOH)_2$, $2H_2O$. Characters, large, colourless, efflorescent, monoclinic crystals, soluble in water.
Dose : 16–60 mg. ($\frac{1}{4}$–1 gr.).

Special Therapeutics.—Oxalic acid is chiefly of interest as a poison; internally, large doses cause severe gastro-enteritis, smaller doses lead to paralysis of the central nervous system. Antidotes are preparations of lime and magnesia. It agrees with other acids in its antiseptic properties, it prevents coagulation of blood by precipitating calcium. Therapeutically it has a limited sphere of action; it has been used with success in sciatica. It is said to be emmenagogue.

Acidum Picricum (B.P.). $C_6H_2(NO_2)_3.OH$. Characters, yellow crystalline needles or scales, soluble in water 1 in 95.
Dose : 6–30 cg. (1–5 gr.).

(*a*) Lotio Acidi Picrici. 1 in 100.
(*b*) Unguentum Acidi Picrici. 1 in 50.

Special Therapeutics.—1 per cent. solutions are useful applications for burns, scalds, etc.; they should be avoided where large areas are affected, as poisoning may result from absorption. Picric acid has also been of service in eczema, erysipelas, pruritus ani, sweating feet, and chilblains. The ointment is better than the solution for burns of the eye, but cocaine should first be instilled.

Acidum Formicum. H.COOH. Characters, colourless liquid with pungent odour, contains 25 per cent. acid.
Dose: 12–60 cl. (2–10 min.).

(*a*) Balneum Formicum Effervescens.

Special Therapeutics.—Formic acid is a muscular stimulant and relieves fatigue, whether given internally or used externally as a bath; it has therefore been used in convalescent and debilitated conditions. Formic acid and sodium formate intramuscularly have produced benefit in muscular rheumatism, gout and paralysis agitans; 10–15 min. of a 2 per cent. solution of the acid are employed, cocaine being given previously to allay the pain consequent on the injection.

Acidum Osmicum. OsO_4. Characters, yellow crystals, soluble in water.
Dose: 0·5–1 mg. ($\frac{1}{120}$–$\frac{1}{60}$ gr.); hypodermic dose of 1 per cent. solution 12–60 cl. (2–10 min.).

Special Therapeutics.—Local injections of osmic acid have been employed with some success over painful spots in trigeminal neuralgia, lumbago, and sciatica; the treatment is painful.

Acidum Hydrofluoricum. HF. Character, colourless fuming liquid which attacks glass.

(*a*) Acidum Hydrofluoricum Dilutum. 0·5 per cent.
Dose: 3–10 dl. (5–15 min.) well diluted.

Special Therapeutics.—Hydrofluoric acid is a powerful antiseptic and corrosive, but its therapeutic value is doubtful. Successful results have been recorded from its internal administration in goitre.

Acidum Pyrogallicum. $C_6H_3(OH)_3$. Characters, light white crystals, soluble in water, discolouring in air.
Dose: 30–90 mg. ($\frac{1}{2}$–$1\frac{1}{2}$ gr.).

(*a*) Unguentum Acidi Pyrogallici. 1 in 8.
(*b*) Unguentum Acidi Pyrogallici Compositum. Contains pyrogallic acid 5 per cent., ammonium ichthosulphonate 5 per cent., salicylic acid 2 per cent., in soft paraffin.

Special Therapeutics.—Pyrogallic acid is strongly antiseptic and irritant; it is used as a stimulant in chronic skin deseases such as psoriasis, lupus, etc., and in ringworm. It is often employed as a hair dye. The skin stains may be removed by ammonium persulphate.

Acidum Trichloraceticum. CCl_3COOH. Characters, colourless, rhombic, deliquescent crystals with pungent odour.
Dose: 12–30 cg. (2–5 gr.).

Special Therapeutics.—It is a valuable and rapid caustic for warts, condylomata, granulations, etc., and is less painful than the ordinary mineral acids; a single crystal on a growth produces at once a white scar which falls off in a few days. Solutions (1 per cent.) are employed as antiseptics for wounds, ulcers, erysipelas, and gonorrhœa. In tonsillitis the application of the acid to the crypts has been found of marked benefit. Internally it has been recommended for gastritis.

Acidum Carbonicum $CO\langle{}^{OH}_{OH}$.

Special Therapeutics.—Carbon dioxide has a stimulant action on the skin causing redness. Effervescing baths (*see* Sod. Bicarb.) have, therefore, been employed to dilate the skin vessels, to lower the blood-pressure and reflexly to stimulate the heart as in the Schott-Neuheim treatment of heart diseases. Gaseous carbon dioxide in small percentages has been advised in spasmodic conditions, and as a restorative; it stimulates expiration, and acts as a cardiac stimulant. Inhalation of the gas has been advocated as a preventative and cure of surgical shock. Internally carbonic acid causes congestion of the mucous membrane of the stomach and augments its muscular activity. The increased vascularity of the mucous membrane promotes absorption, whence the advantage of using effervescing salines as diuretics.

Carbonic Acid Snow.—Solidified CO_2 in the form of pencils is now very largely employed for the destruction of warts, nævi, moles, lupus vulgaris and erythematosus, rodent ulcer, etc. The treatment is known as "refrigeration" or "chrymotherapy." Pencils of carbonic acid snow are prepared from a gas cylinder, and the pencil is pressed on the surface of the growth for periods varying from 5 to 30 or 40 seconds, according to the size and depth of the growth. No caustic effect results, but the area becomes firmer and in 2 to 3 minutes swollen. In half-

an-hour hyperæmia results, and possibly vesication. The ultimate scars are pale, soft and pliable. The treatment is almost free from pain. Good results have been recorded in the treatment of trachoma and corneal ulcers.

W. J. D.

ALKALIES: PHARMACOLOGY AND THERAPEUTICS

The true alkalies consist of the hydroxides, carbonates, and bicarbonates of sodium, potassium, and lithium. Ammonium, although alkaline, possesses the specific actions of the NH_3 group. Alkalies owe their action to the OH group, which is dissociated even from bicarbonates. They have four common properties which form the bases of their principal actions, viz. (1) they neutralise acids, (2) they form soluble alkali-albumens from proteins, (3) they saponify fats, and (4) they dissolve mucus.

External Actions. (*a*) *Caustics.*—Alkalies and to a lesser extent their carbonates act as powerful caustics. They do so by saponifying the oily secretion of the skin, extracting water from the cells, and dissolving the superficial layers as alkali-albumins. Strong solutions or pencils of potassium and sodium hydrate are very powerful in this respect and are liable to penetrate deeply and cause ulceration, since the tissues, being alkaline, have no power to check their progress. They are employed for the removal of warts and other superficial tumours.

(*b*) *Emollients.*—Dilute solutions of the hydrates, carbonates and bicarbonates of potassium and sodium by forming a soapy layer over the skin neutralise any irritant secretions in skin diseases. At the same time since they soften the epithelium they are useful agents in the removal of scabs, sodium bicarbonate being frequently employed for the purpose.

(*c*) *Antiseptics.*—Although not put to much practical use, alkalies are good antiseptics; this is a property of the OH group.

Internal Actions. (*a*) *Mouth.*—The alkalies in dilute solutions act as demulcents, they have a distinct alkaline taste and produce a soapy feeling in the mouth, simultaneously they dissolve the mucus and superficial cells of the mucous membrane and inhibit the secretion of saliva—this latter action is mechanical, *i.e.* lubrication being provided for, saliva is not secreted. They are often useful as mouth washes, particularly where inflammatory reaction has taken place round the neck of a tooth from acid fermentation; a little sodium bicarbonate locally applied immediately abolishes the pain.

(*b*) *Stomach.*—Alkalies act as direct antacids, neutralising excessive formation of hydrochloric acid. They inhibit the secretion of gastric juice, but by dissolving mucus and albumin, they probably aid digestion by permitting more intimate association of the gastric juice with the food. Excess of alkali, of course, delays gastric digestion, and as a lessened acidity of the stomach contents delays the opening of the pylorus, stasis of the contents results. None of the alkalies has any marked action on the stomach muscle; potassium being a muscular depressant, its preparations are not so preferable as those of sodium.

(*c*) *Duodenum.*—Because alkalies diminish the gastric acidity, large quantities may therefore diminish the formation of pancreatic juice. It is improbable that the small doses used in therapeutics have any action in this respect, especially as it has been shown that the acidity of the stomach is kept up to a normal percentage (see Acids). Otherwise they have little action on the alimentary canal from which they are absorbed and pass into the blood stream as carbonates.

(*d*) *Actions on the Blood and on Metabolism.* Alkalies increase the alkalinity of the blood plasma and of the tissues. Small quantities stimulate the movements of leucocytes and cilia, while stronger concentrations paralyse these movements. When perfused through the isolated frog's ventricle, alkalies increase the tone of the heart muscle, diminish diastolic relaxation, and cause ultimately systolic standstill of the organ, which condition is antagonised by acids. Perfusion of alkalies through the vessels leads to contraction of the arteries. Perfusion of the mammalian heart with dilute alkalies causes at first an increased amplitude in the contractions, the rate remaining constant. In a short time, however, complete auriculo-ventricular block occurs and the rate and force diminish till the heart stops in diastole. The coronary arteries are powerfully constricted.

Alkalies have been supposed to exert a marked influence on metabolism from the fact that many oxidative processes progress more rapidly in an alkaline medium. The results obtained by estimations of the nitrogenous excretion in the urine have been discordant and the variations recorded are not striking, therefore we must assume that their action, if any, is transitory and practically negligible. Increased excretion of urea with concomitant diminution of ammonia has been observed. This is due to the fact that the ammonia which is necessary for the neutralisation of acid materials is replaced by the alkalies, and the nitrogen thus set at liberty is formed into urea. There is most probably an increased oxidation of fat brought about by the administration of alkalies, and to this influence is to be ascribed the value of the alkaline waters of Carlsbad and other springs in the reduction of obesity.

Excess of alkali is removed by the excretion

of alkaline salts in the kidney; this results in either a diminution of the acidity or actual alkalinity of the fluid. Unless very large doses be taken repeatedly, the alkalinity is merely transitory. They certainly give relief in cases of gravel, but unless the urine be made neutral or alkaline by their use, the uric acid is not dissolved, but since smaller quantities are undoubtedly of benefit, the action may be due to their diuretic properties and the consequent dilution of the urine. While the alkalies tend to hold the uric acid in solution and prevent its deposition, they have no power to redissolve already formed calculi; the alkaline urates are themselves not particularly soluble and are formed only when the medium is strongly alkaline. Nevertheless alkaline therapy has led to disintegration of urinary concrements, and it is probable that the increased alkalinity serves to dissolve the mucus which binds the particles together. The alkalies are useful in conditions where excessive acidity of the urine gives rise to irritation of the bladder and urethra.

The important question of the value of alkalies in uric acid diathesis and gout is one which is in an unsettled condition. The pathology of these conditions is still debated, but the preponderance of evidence is in favour of a condition of uric acid retention caused by some alteration in the kidney; if this be the case no conclusive evidence has been adduced to prove that alkalies increase the excretion of uric acid. Uric acid, the end product of nuclein metabolism, is a dibasic acid forming neutral and acid salts, the latter of which by combining with another molecule of uric acid form quadriurates. These decompose into free uric acid and sodium biurate which is deposited in the tissues. The older theory of the use of alkalies in these conditions depended on the fact that the biurates of potassium and lithium are more soluble than sodium biurate, and it was expected that by their administration the biurate would be redissolved or at least prevented from deposition; but it has been shown that alkalies cannot prevent or delay the precipitation of sodium biurate from solutions of the quadriurate. It must be admitted that alkalies are clinically of advantage in gouty diathesis, and it is not improbable that their improvement of the disturbances of the digestive system may play a large rôle in their beneficial action.

The alkalies—especially as mineral waters—have long been considered as efficacious in the treatment of diabetes. Critical researches from the clinical side have offered no ground for this belief. They certainly diminish the action of diastase on glycogen but do not influence the glycogen formation in animals. In the last stages of diabetes where the condition of acidæmia from oxybutyric acid has set in, the alkalinity of the blood may be augmented by alkalies with marked benefit, and in more advanced cases—although the treatment is merely palliative—intravenous injections of saline alkaline with sodium bicarbonate produce decided improvement, the patient being thereby temporarily aroused from the coma. The same treatment has been used with success in the last stages of phosphorus poisoning.

(*e*) *Actions on other Functions.*—Alkalies have been credited with the power of increasing and liquefying the bronchial secretion by way of the circulation. There is no evidence that they are excreted in the bronchial glands, and it is doubtful whether the slight and transient increase in the alkalinity of the blood augments the secretion. They have been found useful in the treatment of gall-stones and biliary catarrh, although their effect in these conditions is obscure. The potassium alkalies in particular were employed in the treatment of acute rheumatism, and certain authorities maintain that they are as efficacious as the salicylates. The consensus of opinion, however, is in favour of their being abandoned for this purpose.

Toxicology.—The symptoms of alkali poisoning are principally those of corrosion. There is an acrid caustic taste on swallowing, followed by heat and burning extending from the throat to the stomach, the mucous membrane of the mouth becomes swollen and eroded. Should vomiting occur the material contains shreds of mucous membrane and dark brown blood. Diarrhœa with abdominal pain is a common sequæla; the skin becomes cold and clammy and the pulse feeble. With large doses shock and collapse may lead to death. In cases which recover stricture of the gullet or pylorus may occur later.

Post-mortem.—The mucous membranes are found white and eroded in patches, the lower part of the gullet being most affected. The stomach is generally bright red in colour, and the mucous membrane denuded,

Treatment.—(1) Administer solutions of dilute acids—vinegar, citric, or tartaric.

(2) Give demulcents, such as white of egg, olive oil, or gruel.

(3) Avoid the use of the stomach pump, lest it perforate the corroded walls of the œsophagus or stomach.

Sodii Hydroxidum (U.S.P.). NaOH. Characters, usually in the form of crystalline white pencils, very deliquescent.

(*a*) Liquor Sodii Hydroxidi (U.S.P.). 5 per cent. in water.

Dose: 1 ml. (15 min.) well diluted.

Sodii Ethylas. NaC_2H_5O. Characters, pale, reddish yellow powder, hygroscopic

(*a*) Liquor Sodii Ethylatis. 5 per cent. of Sodium in alcohol, freshly prepared.

Sodii Carbonas (B.P.). $Na_2CO_3, 10H_2O$. Characters, translucent, colourless, efflorescent crystals, soluble in water.

Dose : 3–20 dg. (5–30 gr.) (¼–2 gm.).

(*a*) Sodii Carbonas Exsiccatus (B.P.). Na_2CO_3. White amorphous powder, absorbs moisture, soluble in water.

Dose : 2–6 dg. (3–10 gr.).

(*b*) Balneum Alkalinum. Sodium Carbonate 1–1000

Sodii Bicarbonas (B.P.). $NaHCO_3$. Characters, white, odourless, finely crystalline powder, soluble in water.

Dose : 3-20 dg. (5–30 gr.).

(*a*) Trochiscus Sodii Bicarbonatis (U.S.P.). 2 dg. (3 gr.).

(*b*) Balneum Effervescens. Sodium bicarbonate 0·3; acid sodium sulphate 0·15; sodium chloride 1; calcium chloride 0·15; water to 100. An improvised Nauheim bath.

Special Therapeutics. Sodium hydroxide and Liquor Sodii Ethylatis are useful caustics for warts, nævi, lupus, etc. Sodium carbonate and bicarbonate are employed externally as lotions and baths to allay itching of skin diseases and for the removal of scabs. Their most frequent use is in the treatment of dyspepsia, the bicarbonate being preferable. In hyperacidity and irritative dyspepsia they neutralise excess of acid, and the evolution of CO_2 in the stomach dilates the vessels and improves the muscular movements of the organ. Sodium bicarbonate is often administered in effervescing form in digestive disorders and as a mild aperient; and combined with bismuth carbonate, oxide or salicylate in gastritis and gastric ulcer. Lotions of the carbonate combined with antiseptics are useful as douches in nasal and pharyngeal catarrh.

Potassa Caustica (B.P.). KOH. Characters, hard, white, deliquescent pencils.

(*a*) Liquor Potassæ (B.P.). Contains 5 per cent. KOH.

Dose : 6–18 dl. (10–30 min.) well diluted.

(*b*) Pasta Potassæ et Calcis. Vienna paste. Contains potassium and calcium hydroxides, equal parts.

Potassii Carbonas (B.P.). K_2CO_3. Characters, white, colourless crystalline, deliquescent powder.

Dose : 3–12 dg. (5–20 gr.).

Potassii Bicarbonas (B.P.). $KHCO_3$. Characters, white prisms or granular non-deliquescent powder, with saline alkaline taste, soluble in water.

Dose : 3–20 dg. (5–30 gr.).

(*a*) Mistura Potassii Bicarbonatis. Contains potassium bicarbonate, tincture of hyoscyamus, and camphor water.

Dose : 15-30 ml. (½–1 fl. oz.).

Special Therapeutics.—The alkalies of potassium are used in the same conditions as those of sodium, the potassium salts being preferred in cases of gout and rheumatism. Large doses of the bicarbonate are often given at bedtime to induce alkalinity of the urine during the night, and prevent deposition of uric acid. Vienna paste is occasionally useful as a caustic.

Lithii Carbonas (B.P.). Li_2CO_3. Characters, white, odourless, amorphous powder, soluble in water 1–70.

Dose : 12–30 cg. (2–5 gr.).

(*a*) Aqua Lithiæ. 10 gr. to 1 pint saturated with CO- under pressure.

(*b*) Granulæ Lithii Carbonatis. 3·5. per cent.

Dose : 2–8 g. (30–120 gr.).

Special Therapeutics.—Lithium carbonate and other lithium salts are used internally in the treatment of gout and rheumatism and compresses of saturated solutions are applied locally to gouty joints. The basis of the treatment is that lithium biurate is four times more soluble than sodium biurate.

W. J. D.

SALT-ACTION, WATER AND THE THEORY OF IONS

Various physiological and pharmacological phenomena can be explained by a correct understanding of Salt-Action. An intricate system or series of systems of semipermeable membranes exists throughout the body; the capillaries, the epithelium lining the intestines, the renal glomeruli—to cite a few only. Strictly speaking a semipermeable membrane is one which allows the solvent to pass freely through it, and which prevents the passage of substances held in solution. The adjective, "semipermeable" is, however, capable of somewhat loose application; a membrane may, for instance, be strictly semipermeable to normal saline solution, allowing the water to pass through freely and blocking the passage of the salts held in solution, whilst a similar membrane may be strictly permeable or impermeable to solutions of other substances. In this article the term semipermeable is used in this loose sense, for whilst in the main the solvent passes through and the substances held in solution are prevented from passing through, in practice there is no doubt that part at any rate of

certain substances held in solution can and do pass through these membranes with the solvent. Moreover, a membrane which is semipermeable in the strict sense of the term may after a time allow the passage through it of certain substances held in solution.

To take an example, let us imagine a vessel whose walls are composed of a "semipermeable" epithelial membrane containing a fluid, perhaps blood; and surrounding this vessel a space containing another fluid, possibly lymph. As long as the two fluids on either side of this membrane are isotonic (*i. e.* contain weight for weight the same number of molecules of substances held in solution), the balance is preserved, and there is no exchange of constituents between the two fluids. If, however, a given volume of one of these fluids contains a greater number of molecules than the other, osmosis takes place, water being attracted from the hypotonic to the hypertonic solution, and to a smaller extent substances held in solution leaving the hypertonic for the hypotonic solution, until the two solutions become isotonic. In other words, each substance held in solution exerts its own osmotic pressure, the intervening semipermeable membrane being no strict barrier to the free interchange of constituents between the two solutions. Osmosis, then, is closely allied to diffusion. This process of osmosis is going on continually in the body, and it proceeds whenever two fluids of varying tonicity meet, with only a semipermeable membrane intervening. Generally speaking, the normal body-fluids (blood and lymph) are taken as a standard of tonicity, and fluids entering the body are spoken of as hypertonic or hypotonic, according as their molecular concentrations are higher or lower than that of the blood.

It might be imagined from this that if for any reason the body-fluids became very watery or very rich in substances held in solution, a time would come when either the whole body would become waterlogged with a thin aqueous fluid, or that all the body-fluids might become concentrated solutions; but in the normal animal body such contingencies are prevented by various means. Firstly, the process of osmosis is so general throughout the body that if for any reason the blood should become very watery, this departure from the normal is soon rectified by osmosis between it and the lymph; and should this render the lymph very dilute, further osmosis will take place, fluid exuding into the serous cavities, intestines, etc., whilst the kidneys supply an efficient safety-valve for any excess of the soluble constituents of the blood or for an excess of water. It is highly probable that vital activity plays no inconsiderable part in helping the organism to maintain the composition of the body-fluids at or near the normal, so that osmosis alone does not, perhaps, account for the whole process. Thus, if there is a tendency for the body-fluids to become dilute, water will be excreted into the lumen of the intestine and also by the kidneys and sweat-glands, whilst an appetite will be created for foods rich in those salts in which the body-fluids are deficient. Similarly, if for any reason the body-fluids become concentrated, the amount of fluid excreted becomes small, and if osmosis cannot supply this deficiency, actual or relative, of water, on account of a general poorness in water of all the body-fluids, thirst is induced and the organism takes in water by the mouth, which after absorption will dilute the blood and lymph, when osmosis will be set up in the reverse direction until the balance is restored, and the composition of the body-fluids has again reached the normal.

It will be seen, then, that whilst osmosis may not perform all these functions unaided, it is a process that aids considerably in the preservation of the balance of the constitution of the body-fluids; moreover, it is a process that is entirely physical as opposed to the vital processes: and therein lies its great importance to the organism, for an entirely physical process can go on passively, whilst a vital process entails the absorption and utilising of oxygen; in other words, it is a drain on the energy of the organism. So that the greater the amount of work that can be done in the economy by osmosis, the less will vital processes be called into play, and the less energy will be wasted that might be employed usefully in other directions; thus the process of osmosis may be said to be a great conservator of energy, enabling the organism to exist with less respiratory interchange and less metabolism generally than would be the case if it had to rely solely on vital processes.

This preliminary consideration brings us to two of the subjects mentioned at the head of the chapter, viz. salt-action and water.

Salts and water are amongst the most important substances concerned in this process of osmosis. It is true that other substances as well play a part, such as sugars and urea. Now salt-action pure and simple is not concerned with any vital processes, but with the purely physical process of osmosis.

Any tissue placed in an isotonic solution of the normal body-salts (*i. e.* in normal saline solution) preserves its normal functions for a considerable time, though all connections with the organism are severed. Tissues placed in hypotonic salt solutions absorb water from the medium in which they are placed, and swell

up till they reach a condition which might be described as œdematous. Similarly, if placed in hypertonic solutions, the tissues lose water to the surrounding medium, and become, so to speak, shrivelled, hard and dry. These changes can easily be observed by placing red blood corpuscles in isotonic, hypotonic and hypertonic salt solutions, and observing the changes under a microscope, when it will be seen that in the first case no change takes place in the cells, in the second case they become swollen and spherical, and in the third case they shrink and become crenated.

Water acts in an exactly similar way, for every body-fluid is a saline solution; and if we introduce water into any normal saline solution it will render that solution hypotonic. Thus salts and water may be regarded to a certain extent as antagonists; salts introduced into the body rendering the body-fluids hypertonic, and producing an osmotic pressure in one direction, whilst water similarly introduced renders the body-fluids hypotonic and induces osmotic pressure in the reverse direction.

Before proceeding further with the discussion of salt-action it will be well to consider briefly the Theory of Ions. According to this theory, all salts consist of two ions, the positive and negative. In the normal dry state each molecule of a salt is electrically neutral; but as soon as these molecules enter into solution they become split up into their constituent ions or electrons, the positive ions or kations and the negative ions or anions. If an electric current be passed through such a solution, the positive ions become attracted towards the positive pole, and the negative towards the negative, when they lose their ionic form and undergo chemical change, becoming electrically neutral.

All salts do not ionise to the same extent, and dilute solutions of a salt ionise to a greater extent than do concentrated solutions of the same salt. Moreover, solutions which do not ionise at all are not conductors of electricity (such as solutions of urea and of sugars); and the conductivity of a solution towards an electric current varies directly as its power of ionisation.

An intimate relation exists between this ionic theory and the phenomenon of osmosis. It has been found that the osmotic power of a solution varies directly with the number of molecules in solution. Thus if a 5 per cent. solution of urea (a substance which does not ionise) has an osmotic power of x, a 10 per cent. solution of this substance will have an osmotic power of $2x$. If now, for the sake of example, a 1 per cent. solution of NaCl has the same osmotic power as the 5 per cent. solution of urea (*i. e.* an osmotic power of x), it will be found that a 2 per cent. solution of NaCl has an osmotic power of considerably more than $2x$. This apparent contradiction to the axiom just enunciated is explained by the supposition that the NaCl molecule ionises, and each of the ions into which each molecule splits up has the same osmotic power as the original whole molecule. So one can understand what powerful osmotic agents certain inorganic salts can be, as compared with substances which do not ionise.

Having thus briefly enunciated the elements of the ionic theory, we can return to the subject of salt-action. It is known that the actions of many salts are due to one or other of the ions, and not to the whole molecule. Thus, in a sedative mixture one prescribes the bromide of sodium, not because the effect of the sodium is desired—it is practically valueless as an active pharmacological agent—but because one desires to give the patient the benefit of the bromide ion; or again, knowing that the sulphate ion acts as a saline purgative, one does not prescribe Atropine Sulphate for that purpose, for in this case the Atropine ion is by no means inert; its action would, indeed, quite overshadow that of the sulphate ion; one gives instead the sulphate ion combined with a practically inert positive ion.

With these considerations before us, we can see at once that for many purposes one can select at will the most suitable salt for any given purpose. Various points in this connection must be considered; it may be desirable that the salt to be administered be absorbed slowly, as, for example, in the case of a saline purgative: on other occasions rapidity of absorption is desired: again, for some purposes it may be well to have one of the radicles in the form of an inert ion, in order that the effect of the other ion alone may be exerted: or again, each ion of a salt may help towards the same end, as is seen in the case of the saline purgatives, where the salt that produces the most efficient action is Magnesium Sulphate. Here the action is one of osmosis, and the desideratum is to get as much water poured into the intestine as possible; therefore, *cæteris paribus*, the salt which is most slowly absorbed from the intestine will be the one to choose; and this salt is found to be Magnesium Sulphate; Magnesium taking longer to be absorbed than Potassium, Sodium, etc., whilst chlorides, bromides, nitrates, etc., are all absorbed more quickly than are sulphates. The reason why certain ions are absorbed quickly and others slowly is not known.

Whilst some ions, such as Na and Cl, are practically inert, others may be described as having almost specific actions on various tissues; thus Barium has a special affinity for

muscle, whilst Bromine and Iodine have a more or less selective action on nerve-cells.

The chief pharmacological action of salts, however, is that of inducing osmosis; by this means fluid can be removed from one part of the body to another, and so indirectly diuresis and catharsis can be brought about. The simplest illustration of this action is afforded by introducing a concentrated solution of Magnesium Sulphate into the intestine. This salt, as already pointed out, is but slowly absorbed, so that the bulk of the salt will remain in the lumen of the intestine, the result being that, as this mass of hypertonic solution passes downwards, water is continually passing into the lumen of the intestine from the surrounding tissues by osmosis, and would continue to do so until the Magnesium Sulphate solution had been rendered isotonic. The result of this is that the intestine comes to contain a large bulk of fluid contents, which stimulates peristaltic action, and at the same time softens the fæcal contents. Any other salt will act in the same way if enough of it is given; but, naturally, the faster a salt is absorbed from the intestine, the more of that salt must be given in order that enough may be left within the lumen to produce sufficient osmotic action for the purpose of catharsis.

Similarly, any salt will produce diuresis, but here it is desirable that the bulk of the salt should find its way into the blood stream; therefore the salt must be one that is easily absorbed from the intestines; moreover, it is desirable that the salt, as given by the mouth, should be in isotonic or hypotonic solution, otherwise, before it can be absorbed, fluid will have to be withdrawn from the tissues into the intestine, in order to induce an osmotic pressure in the right direction. Given suitable conditions, then, the salt is absorbed into the blood, where it exerts its osmotic power and attracts water from the surrounding tissues, producing a condition of hydræmic plethora—exactly the same result as would be obtained by injecting isotonic solution directly into the blood stream. The result of this is a dilatation of the renal vessels with a copious flow of pale urine of low specific gravity. Though, speaking generally, one may say that the diuretic power of salts varies directly with the rapidity of absorption, and their cathartic power inversely with that rapidity, this does not prove to be always the case; it is found, for example, that Sodium Sulphate is a far more efficient diuretic than Sodium Chloride, though the latter is absorbed more quickly than the former. It may be that the sulphate, which, as compared with the chloride, may be regarded as a foreign body in the blood, directly stimulates the renal epithelium; or it may be that this very property of slower absorption produces a freer flow of urine simply because its action is more prolonged.

It can be easily understood that water will produce exactly similar effects: water, being a hypotonic fluid, will be quickly absorbed from the intestine, and will produce hydræmic plethora with a resultant increase in diuresis. Unless enormous quantities of water are given, so little will remain in the intestine that diuresis must be the ultimate effect produced rather than catharsis. One curious point may be noticed with regard to the effect of water as a diuretic—when water is given by the mouth, it produces a more rapid and more copious flow of urine than is produced by injecting the same quantity of water either subcutaneously or intravenously. That some factor other than simple osmosis is at work is obvious. It is possible that the water, during the process of absorption from the gastro-intestinal tract, takes up some substance which either directly or indirectly stimulates the renal epithelium to activity.

Salts have a distinct advantage over water as diuretics, in that they produce the condition of hydræmic plethora by abstraction of water from the tissues, the consequence being that as soon as the initial increase in diuresis has subsided, a condition of thirst is created by the loss of fluid from the tissues; more fluid is therefore imbibed, which in most cases more than makes up the deficiency, with the result that a second increase in diuresis takes place.

It is a matter of common experience that the ingestion of foods rich in salts, such, for example, as the kippered herring of the breakfast-table, provoke intense thirst. The salt after absorption renders the blood temporarily hypertonic; fluid is therefore abstracted from the tissues to compensate for this hypertonicity, and an increase in diuresis takes place. A feeling of thirst ensues, which in nine cases out of ten is gratified at once; and again, in nine cases out of ten more fluid is imbibed than is necessary to compensate for this loss of fluid by the tissues, the result being a further increase in diuresis. Nature, then, has so arranged matters that, given opportunities for freely quenching thirst, the fluid equilibrium of the tissues will be maintained. When the tissues are actually or relatively poor in fluids, the animal drinks water; when the tissues are rich in fluids, the animal does not drink. This is the natural sequence, and, of course, does not apply to the vagaries of those individuals who habitually indulge in alcoholic drinks, many of whom appear to drink at all times, whether a feeling of thirst is present or not!

To repeat what was hinted at earlier in this chapter—salt-action alone is probably not entirely responsible for the maintenance of the

equilibrium of the tissue-fluids: the kidneys and possibly other organs help considerably in maintaining the correct balance. Richet has postulated that: "Le rein a pour fonction d'expulser les substances dialysables anormales du sang, que ces substances soient anormales par leur nature chimique propre ou par leur excès." That this function of the kidney is not entirely brought about by the purely physical process of osmosis is probable, if for no other reason, from the fact, pointed out by Grijns, that during diuresis provoked by sugars and by salts the temperature of the urine frequently rises to a point higher than the temperature of the blood. This certainly lends support to the theory that the kidney is doing active work.

The chloride of sodium may be taken as an example of a salt which is pharmacologically active solely on account of the salt-action induced by its ingestion, for neither the Na ion nor the Cl ion has any notable specific action; also it must not be forgotten that this is the salt which forms the bulk of the soluble constituents of the normal body-fluids.

Sodii Chloridum ($NaCl$), white cubical crystals, soluble in water 1 in 3. Dose, ½–1 oz.

D. C.

CERTAIN NEGATIVE IONS

Acetates, Nitrates, Sulphates, Phosphates, Tartrates, Citrates, Hypophosphites, Sulphites, Chlorates, Oxalates

As has been shown in the chapter on the Ionic Theory, the action of a salt may be due entirely or almost entirely to either the positive or the negative ion. In this chapter the actions of certain negative ions will be discussed, regarding these negative ions as separate entities which have definite pharmacological actions of their own, without reference to the positive ions with which they may be combined in the form of salts for the purpose of administration. It must be borne in mind that in some of these combinations the action of the negative ion is paramount, whilst in others, as for example in the case of Atropine Sulphate, the action of the negative ion is so weak as compared with that of the positive ion that its action may be disregarded.

Acetates.—The acetate ion has no more of a specific action than has the chloride ion, which, as was shown in the chapter on Salt-Action (*q.v.*), owes its activity entirely to salt-action. Acetates are absorbed rapidly from the intestinal canal. After absorption they are oxidised in the tissues, with the formation of carbonates, only a minute proportion of the acetate being excreted as such. The carbonates formed by the oxidation of the acetates render the blood more alkaline, and consequently an alkaline urine results, from the excretion of the carbonates by the kidneys. Moreover, as a result of this excretion of the carbonates by the kidneys, an increased flow of urine takes place. Acetates, then, act as efficient diuretics.

By the oxidation of the acetate, which takes place in the tissues, a certain amount of energy is set free. In practice, however, the acetates cannot be looked upon as being capable of taking the place of natural foodstuffs; for the amount required for this purpose would induce a considerable degree of gastric irritation: moreover, the salt-action consequent on the ingestion of a large amount would upset the equilibrium of the body-fluids by the osmosis induced.

Sodii Acetas, ($CH_3COONa.3H_2O$). Colourless crystals, soluble in water 1 in 1. Dose, 10–20 gr.

Potassii Acetas, (CH_3COOK). Deliquescent white crystals, soluble in water 2 in 1. If prescribed in mixtures with quinine, an insoluble acetate is formed. Dose, 15–60 gr.

Liquor Ammonii Acetatis.—Ammonium carbonate 1 part, water 20 parts, with enough acetic acid to neutralise: should be freshly prepared. Dose, 2–6 fl. dr.

Nitrates.—It has been stated that nitrates have no more specific action than the chlorides; this statement, however, is probably incorrect. In the first place, chlorides are a natural constituent of the body, whilst nitrates are not; moreover, very much weaker solutions of nitrates than of chlorides will produce gastro-intestinal irritation; so that, in all probability, nitrates have some specific action.

If given in dilute solution by the mouth, the irritation is unnoticeable, and the nitrates are easily absorbed. It has been suggested that after absorption, nitrates are reduced to nitrites, but this appears improbable, since no nitrite action has been observed. However, the fate of the nitrates after absorption is unknown. Probably a certain proportion is excreted in the urine and some in the saliva and sweat; the remainder may be broken down, and the nitrogen given off by the lungs in gaseous form.

Nitrates are used as diuretics and diaphoretics. The increased diuresis resulting from the ingestion of nitrates is probably due in part to salt-action pure and simple, and partly to a direct or indirect action on the renal epithelium.

Sodii Nitras, ($NaNO_3$). Chili Saltpetre. Dose, 5–30 gr.

Potassii Nitras, (KNO_3). Nitre or Saltpetre—colourless crystals having a saline taste, easily soluble in water. "Sal Prunella" balls consist of fused potassium nitrate. Should be given in dilute solution only. Dose, 5–20 gr.

Charta Potassii Nitratis, Bibulous paper impregnated with a strong solution of potassium

nitrate, which, when ignited, smoulders, giving off dense fumes of smoke containing pyridine bodies: these are sometimes useful in relieving asthmatical spasms.

Sulphates.—The sulphate ion owes its activity entirely to salt-action; that is to say, the sulphates as such have no specific action. Sulphates are absorbed but slowly from the alimentary canal; consequently the salt-action of these salts will not be particularly effective in producing increased diuresis if the salt be given by mouth. Under these conditions sulphates form the saline cathartics *par excellence,* the reason being that, owing to the slowness with which they are absorbed from the alimentary canal, the bulk of any given dose has time during its passage down the intestine to attract fluid into the lumen of the intestine by osmosis; whereas a salt which is more readily absorbed has no time to attract any considerable volume of fluid into the lumen of the intestine, by reason of the very rapidity of its absorption.

On the other hand, when injected directly into the circulation, sulphates form very efficient diuretics, far more efficient than equal quantities of chlorides, for instance. The probable reason for this is that the sulphate is slow of excretion by the renal epithelium as compared with other salts; and therefore, remaining longer in the blood, has more time to attract fluid from the tissues into the blood stream by osmosis; in consequence, a greater degree of hydræmia is induced, which in turn is followed by a more copious flow of urine.

Many of the sulphates are excreted in combination with bodies of the aromatic series, in the form of ethereal sulphates. In this way the sulphates are of importance in the economy, in that they neutralise certain putrefactive products: about one-tenth of the total sulphates in normal urine is so combined, the remaining nine-tenths being in the form of inorganic sulphates.

The readiness with which these aromatic bodies combine with sulphates has been made use of in cases of carbolic acid poisoning, when the sulphate of magnesium or of sodium is given, in order that the phenol may be converted into ethereal sulphate.

Sodii Sulphas, syn. Glauber's Salt, ($Na_2SO_4.10H_2O$). Transparent efflorescent crystals with a bitter taste, soluble in water 1 in 3. Dose, 150–240 gr. as a single dose, or 30–120 gr. for repeated administration.

Potassii Sulphas, (K_2SO_4). Soluble in water 1 in 10. Dose, 15–45 gr.

Magnesii Sulphas, syn. Epsom Salts, ($MgSO_4.7H_2O$). Soluble in water 1 in 1½. Dose, ¼–½ oz. as single dose, or 30–90 gr. for repeated administration.

Sodii Sulphas Effervescens. A mixture of sodium sulphate with sodium bicarbonate, tartaric and citric acids, which mixture effervesces when mixed with water. Dose, 150–240 gr. as a single dose, or 60–120 gr. for repeated administration.

Magnesii Sulphas Effervescens. A mixture of magnesium sulphate with sodium bicarbonate, tartaric and citric acids. As in the case of the effervescent sodium sulphate, the addition of water produces effervescence. Dose, ½–1 oz. as a single dose, or 60–180 gr. for repeated administration.

The sulphates should not be administered except in dilute form, certainly not in greater concentration than 5–10 per cent.

Phosphates.—All that has been said with regard to the sulphates applies with somewhat less force perhaps to the phosphate ion. It depends for its activity on salt-action: it is but slowly absorbed, so that when given by the mouth it acts as a purgative rather than as a diuretic (*vide* chapter on Salt-Action). If injected directly into the circulation, on the other hand, it acts as a diuretic. In neither case is its action so strongly marked as that of the sulphate ion, for its slowness of absorption is less prominent; nevertheless as compared with other ions it is but slowly absorbed.

Certain organic phosphates, particularly the glycerophosphates, have been recommended for use as tonics in certain wasting diseases on the supposition that they would help in the formation of lecithin. All the evidence at our disposal, however, points to the fact that before absorption they are converted into inorganic phosphates, so that they can have no advantage over the inorganic phosphates as therapeutic agents.

Sodii Phosphas, ($Na_2HPO_4.12H_2O$). Colourless crystals or white granules with alkaline reaction, soluble in water 1 in 6. A less efficient cathartic than sodium or magnesium sulphate, but often preferred on account of its tastelessness. Dose, 150–240 gr. as a single dose, or 30–120 gr. for repeated administration.

Sodii Phosphas Acidus, (Dihydrogen Sodium Phosphate). ($NaH_2PO_4+H_2O$). Soluble in water about 1–1 is used to increase the acidity of the urine. Dose 30–60 gr.

Ammonii Phosphas. Dose, 5–20 gr.

Sodii Phosphas Effervescens. A mixture containing sodium phosphate, sodium bicarbonate, citric and tartaric acids, which, when water is added, effervesces. Dose, 150–240 gr. as a single dose, or 60–120 gr. for repeated administration.

Tartrates.—The tartrate ion appears to occupy a place midway between the sulphate ion on the one hand and the chloride ion on the other: the former is hardly absorbed at all, the latter

is readily absorbed; consequently the tartrate will prove to be a less efficient cathartic and a more active diuretic than the sulphate, whilst it is a better purgative and a less powerful diuretic than the chloride. Tartrates as such have no specific action: both catharsis and diuresis being due to salt-action only. After absorption the tartrate is partially oxidised to carbonate, and is excreted in the urine, partly in the form of tartrate and partly as carbonate, the latter rendering both blood and urine slightly alkaline.

Potassii Tartras, $((CHOH)_2(COOK)_2H_2O)$. A crystalline powder with a bitter taste, soluble in water 5 in 3. Dose, 30–240 gr.

Potassii Tartras Acidus, Potassii Bitartras, syn. Purified Cream of Tartar $((CHOH_2COOK.COOH)$. Dose, 15–60 gr.

Soda Tartarata, Potassii et Sodii Tartras, syn. Rochelle Salt $((CHOH)_2.COONa.COOK.4H_2O)$. Colourless crystals, soluble in water 1 in $1\frac{1}{2}$. Dose, 120–240 gr.

Pulvis Sodæ Tartaratæ Effervescens, Pulvis Effervescens Compositus, syn. Seidlitz Powder. The "blue packet" contains 115 gr. of Rochelle Salt with 38 gr. of sodium bicarbonate; the "white packet" contains 38 gr. of tartaric acid. Dose, one each of the blue and white packets in a tumblerful of water, to be taken while effervescing.

Citrates.—Citrates very closely resemble tartrates in their action. They are but slowly absorbed from the gastro-intestinal tract, and in consequence the salt-action set up by their ingestion produces catharsis rather than diuresis. That part of the citrate which is absorbed is oxidised in the tissues very much more readily than is the tartrate. Indeed, practically all the citrate which is absorbed is excreted in the urine as carbonate. This rapid oxidation of the citrate is made use of to render the blood and, consequently, the urine, more alkaline in gouty and rheumatic complaints. Very small doses of the citrate, far short of the amount required to produce catharsis, are sufficient.

If added directly to the blood the citrates form calcium citrate and delay the clotting of the blood.

Sodii Citras, $(2C_3H_4(OH)(COONa_3.11H_2O)$. Whitish, granular crystals, soluble in water 1 in 3. Dose, 10–60 gr.

Potassii Citras, $(C_3H_4(OH)(COOK)_3.H_2O)$. A white crystalline powder. Dose, 15–60 gr.

Lithii Citras, $(C_3H_4OH(COOLi)_3.4H_2O)$. A white crystalline powder, soluble in water 1 in 2. Dose, 5–10 gr.

Lithii Citras Effervescens. Contains lithium citrate 1 in 20. Dose, 1–2 dr.

Liquor Ammonii Citratis. Dose, 2–6 dr.

Sodii Citro-Tartras Effervescens. Dose, 60–120 gr.

Magnesii Citras Effervescens. A mixture of magnesium carbonate, sodium bicarbonate, citric acid and sugar. Dose, 1–3 dr.

Liquor Magnesii Citratis. Magnesium carbonate 15, citric acid 33, syrup of citric acid 60, potassium bicarbonate $2\frac{1}{2}$, water to 360. Dose, 5–12 fl. oz.

Hypophosphites.—The hypophosphite ion has probably no specific action *per se*, though the hypophosphites have been and are very widely used, with the idea that they are of use to the organism in cases of malnutrition from any cause; the supposition being presumably that the hypophosphite was reduced to the phosphate in the tissues. But this cannot be the case, since practically the whole of the hypophosphite can be recovered as such from the urine. All that can be said is that the hypophosphites are readily absorbed, and that the probability is that any beneficial action which has been claimed for them is entirely owing to the iron or calcium with one or other of which they are generally combined, possibly helped by the sugar which is ingested at the same time, the hypophosphites generally being prescribed in the form of the syrup.

Sodii Hypophosphis, $(NaPH_2O_2)$. A white granular deliquescent salt with a bitter taste, soluble in water 1 in 0·6. Dose, 3–10 gr.

Calcii Hypophosphis, $(Ca(PH_2O_2)_2)$. A white crystalline salt with nauseous taste, soluble in water 1 in 7. Incompatible with oxidising agents and with potassium iodide. Dose, 3–10 gr.

Potassii Hypophosphis, (KPH_2O_2). A deliquescent white granular powder with nauseous taste, soluble in water 1 in 1. Incompatible with oxidising agents and with potassium iodide. Dose, 1–6 gr.

Ferri Hypophosphis, $(Fe(PH_2O_2)_3)$, syn. Ferric Hypophosphite. A white amorphous powder with chalybeate taste, sparingly soluble in water; the presence of potassium citrate in the solution renders it more soluble. Dose, 1–5 gr.

Syrupus Hypophosphitum. Contains hypophosphites of calcium 45, potassium 15, sodium 15, with dilute hypophosphorous acid 2, sugar 650, tincture of fresh lemon-peel 5, water to 1000. Dose, 1–2 fl. dr.

Syrupus Hypophosphitum cum Ferro. Contains syrup of hypophosphites, lactate of iron and potassium citrate. Dose, 1–2 fl. dr.

Liquor Ferri Hypophosphitis Fortis. Dose, 10–30 minims.

Syrupus Hypophosphitum Compositus. Contains hypophosphites of iron, manganese, calcium, potassium and sodium, together with sodium citrate, dilute hypophosphorous acid, quinine and strychnine. Each fluid drachm contains approximately $\frac{1}{120}$ gr. of strychnine hypophosphite. Dose, 1–2 fl. dr.

Sulphites.—The sulphites are but rarely employed in therapeutics: when they are used it is chiefly in the form of mild antiseptic mouth-washes, or as a gastric antiseptic. They owe their antiseptic power to their property of withdrawing oxygen from organic matter, being themselves converted thereby into sulphates.

Sulphites are probably but slowly absorbed from the gastro-intestinal tract; at all events, comparatively large quantities when given by the mouth exert but slight toxic effects as compared with very small quantities injected intravenously. The toxic effects consist of a paralysing action on the medulla oblongata, and a poisoning of plain muscle. If too large a dose is given by the mouth, nausea and vomiting may follow, owing to the liberation of sulphur dioxide. Practically all the sulphite which is absorbed is excreted by the kidneys as sulphate. Most samples of sulphites contain a considerable admixture of sulphate.

Sodii Sulphis, ($Na_2SO_3.7H_2O$). Colourless efflorescent crystals, soluble in water 1 in 4. Incompatible with acids. Dose, 5–20 gr.

Sodii Bisulphis, ($NaHSO_3$). A white powder smelling of sulphurous acid, soluble in water 1 in 4. Incompatible with acids. Dose, 5–30 gr.

Sodii Hyposulphis, ($Na_2S_2O_3.5H_2O$). Crystals with a saline taste, soluble in water 1 in 1. Dose, 10–60 gr.

Chlorates.—The chlorates have been used for a long time in therapeutics as local applications to septic conditions of the mouth and pharynx. It was at one time supposed that the chlorates supplied nascent oxygen to the tissues, and that the chlorate was reduced to the chloride. That this is not the case is shown by the fact that after absorption an overwhelming proportion of the amount ingested is excreted as the chlorate in the urine. In spite of this fallacy, however, the chlorates have their uses in septic conditions of the pharynx, and for two reasons: firstly, part of the chlorate is excreted in the saliva, and consequently the septic parts are kept bathed with a dilute solution of the salt; secondly, although the normal tissues may not be capable of reducing the chlorate, the presence of putrefying organic matter does to a certain extent carry out this reduction, with a consequent liberation of free oxygen, which has a weak antiseptic action.

When given by the mouth the chlorates are rapidly absorbed; they have a saline taste, which remains perceptible for a long time, owing to a portion of the salt being excreted in the saliva. Large doses may produce nausea and vomiting owing to salt-action. Again, after absorption there is an increase in diuresis, which is probably attributable to salt-action. The bulk of the salt is excreted in the urine, whilst a smaller quantity is eliminated in the saliva, the sweat and the milk.

Certain individuals appear to have what amounts to an idiosyncrasy for the chlorates; a form of chlorate poisoning having been frequently observed. This consists essentially in the conversion of the hæmoglobin of the blood into methæmoglobin. A series of symptoms directly or indirectly connected with this change may be observed. Following the formation of methæmoglobin a number of the red blood corpuscles break up, producing methæmoglobinuria. If this formation of methæmoglobin is at all massive, the remaining amount of hæmoglobin may be insufficient for the adequate supply of oxygen to the tissues, and a condition of asphyxia supervenes. Furthermore, mechanical obstruction to the excretion of urine may occur from the blocking of the renal tubules with the debris of the broken-down corpuscles. To such an extent may this be carried that anuria may supervene, followed by death from uræmia.

It should be borne in mind that in the dry state and in contact with reducing substances, the chlorates are explosive, and should be treated with due precautions.

Potassii Chloras, ($KClO_3$). Colourless crystals with a saline taste, soluble in water 1 in 16. Incompatible with oxidisable substances, ferrous salts, sugars, nitrites, calomel, hypophosphites, potassium iodide. Contra-indicated in conditions of nephritis. Dose, 5–15 gr.

Trochisci Potassii Chloratis. Made up in lozenges containing 3 gr.

Sodii Chloras, ($NaClO_3$). Colourless crystals with a saline taste, soluble in water 1 in 2. Dose, 10–30 gr.

Oxalates.—The oxalates are not employed in therapeutics: they are powerful poisons to all forms of protoplasm which contain calcium, and therefore to all living animal tissues. It is generally stated that, apart from the affinity of the oxalates for calcium, there is a specific toxicity towards protoplasm; though certain moulds and other low forms of life, many of which contain no calcium, are unaffected by the oxalates.

Oxalates are contained in certain forms of vegetable foods, such as strawberries, rhubarb and spinach. They have an irritant action on the gastro-intestinal tract, and are but slowly absorbed. After absorption, or if injected directly into the tissues, they combine with calcium, and are excreted in the urine as the "envelope crystals" of calcium oxalate.

Oxalates prevent the coagulation of the blood

both *in vivo* and *in vitro* ; also in the presence of oxalates rennet ferment will not coagulate milk.

Use is made of this affinity of the oxalates for calcium in cases of oxalic acid poisoning; the antidote is lime, which, if given within a short time of the ingestion of the poison, forms the insoluble calcium oxalate, and so prevents absorption. Copious draughts of water with or without diuretic salts should also be given, in order that the free flow of urine resulting therefrom may prevent an accumulation of the calcium oxalate crystals in the urinary tubules. D. C.

THE HALOGEN GROUP

This group, which consists of fluorine, chlorine, bromine and iodine, obtained its name from the similarity of its salts to those found in sea salt (ἅλς = the sea). The prominent physical characteristics which distinguish the group suggested the names of the three last members of the group, and denote either a colour or the irritant effects, thus greenish yellow (χλωρός), a smell (βρωμός), and violet-like (ἰώδης). Chlorine, a greenish-yellow gas, is soluble in half its bulk of water; bromine, a heavy volatile fluid or reddish-brown vapour, is soluble in thirty volumes of water; and iodine, a dark metallic-looking solid, is soluble in from 5000 to 7000 parts of water. and they are all soluble in alcohol, ether and chloroform. They are all three strongly irritant, and they have so strong an affinity for hydrogen that they can decompose water and liberate its oxygen. They readily decompose sulphuretted hydrogen and alkaline sulphides, rendering them odourless, and they cause the disintegration of organic matter, diminishing activity of ferments and inhibiting the growth of micro-organisms.

The members of the group for these reasons act as deodorisers, irritants on contact, antiseptics and disinfectants, indirectly oxidising the various substances by chemical action. They also destroy colouring matters and can enter into loose combination with protein substances, and if in sufficient concentration they destroy the vitality of the tissues with which they come into contact.

The compounds of iodine are less stable than those of bromine, while those of chlorine are the least easily broken up.

Bromine and iodine are transformed by alkalies to mixtures respectively of bromates and bromides, and iodates and iodides, in which forms, as well as in the forms of combinations with albumen, they are absorbed and circulate in the blood. These compounds are liable to decomposition by various agencies, notably by acids, and by oxidising substances, the process resulting in the production of free bromine and free iodine respectively. The bromates and iodates, being the more readily decomposed by acids than are the corresponding bromides and iodides, are somewhat more active pharmacologically. The effects produced by bromine and iodine after absorption, then, differ from those produced by the administration of bromides and iodides rather quantitatively than qualitatively.

Bromine and iodine are much more soluble in watery solutions of potassium bromide and potassium iodide than they are in water, and when brought into contact with salts of the heavy metals or with soluble salts of alkaloids form insoluble compounds with them. They also form easily dissociated compounds with starch, the iodide being blue and the bromide orange yellow. This reaction is taken advantage of, together with the fact that chlorine can displace bromine and iodine from their compounds, to identify them. The uncombined halogens are mainly used for their contact actions and may be considered first.

Chlorine.—The solution of the gas in water is of too uncertain strength to be a dependable preparation, and the gas itself is usually prepared when it is required by decomposing one of its compounds at the time. *Calx chlorinata*, $CaCl_2O_2CaCl_2$, is a dull greyish-white deliquescent powder, partially soluble, which yields not less than 30 per cent. of chlorine "available" when treated with an acid. When one part of this is shaken with ten parts of water a solution is obtained yielding from 2 to 3 per cent. (*Liquor Calcis Chlorinatæ*). When mixed with carbonate of sodium and water, the solution known as *Liquor Sodæ Chlorinatæ* is obtained, yielding not less than 2·5 per cent. of available chlorine, rather more stable and sometimes used for internal administration in doses of from 10 to 20 minims.

A very usual non-official means of prescribing chlorine in solution, as a gargle for example, is to order potassium chlorate to be decomposed by hydrochloric acid and the solution to be diluted.

Liquor Chlori Compositus is of this nature, contains about 0·4 per cent. of chlorine and must be freshly prepared. Gargarisma Chlori is a similar preparation.

As the most volatile, most soluble, most easily obtainable and least expensive halogen, it has advantages for purposes of disinfection and deodorisation. Its bleaching properties and its irritant properties, however, are disadvantages, the latter rendering it dangerous. Spasm of the glottis, a feeling of suffocation and severe irritation of the mucous membrane of

the respiratory passages and alimentary canal, follow on the inhalation of the gas in concentration, and redness and even inflammation of the skin may follow the application of it to sores. One part in 100,000 may cause severe pulmonary and bronchial irritation if the action is prolonged.

The treatment of poisoning by chlorine is obviously to neutralise the acids produced and allay the irritation by emollients, and the pain by sedatives and narcotics.

Bromine. — The physical characteristics of this substance, viz., its being less volatile and its being less soluble in water, account for its penetrating the tissues less readily than chlorine, but it can be applied in greater concentration. It can cause greater irritation, therefore, which counter-balances its slightly greater activity as a germicide, which may be expressed approximately as 2 : 3. Thus 2 parts of bromine in 1000 parts of air in presence of moisture will kill spores in a few hours, whereas the necessary concentration of chlorine under similar conditions is 3 in 1000. The contact actions for which it might be used may be obtained more conveniently by chlorine on the one hand or by iodine on the other.

Iodine.—The peculiar properties of the halogen iodine are its solidity, its colour and its solubility. It should contain no moisture (but should give a clear solution in chloroform) or mineral matter (it should sublime without residue). It is sparingly soluble in water, but freely in rectified spirit or in a solution of iodide of potassium in water. Two solutions are official—*Tinctura Iodi Fortis*, containing 10 per cent. of uncombined iodine and 6 per cent. of iodide of potassium, and *Tinctura Iodi Mitis*, containing 2½ per cent. of uncombined iodine and 2½ per cent. of iodide. The proportions of water in these preparations are 10 per cent. in the former, and 2½ per cent. in the latter. The U.S.P. tincture contains 7 per cent. of iodine.

Unguentum Iodi is a 4 per cent. ointment of iodine with iodide of potassium, glycerine and lard, intended to be used where rapid penetration is desired, and there is a similar ointment in the U.S.P.

The so-called decolorised solutions of iodine do not contain uncombined iodine but are solutions of iodides and iodates.

Pharmacology.—It is toxic to any tissue with which it comes in contact, but penetrates slowly and will not injure the tissues in solutions of greater strength than are necessary for the purpose of destroying micro-organisms. A solution of 1 in 500 parts is an efficient antiseptic and bactericidal application, but the expense of iodine (about 13*s*. per lb.) prohibits its use on a large scale.

When applied to the skin it imparts a brown stain which is evanescent if the solution is dilute. When in greater concentration the stain persists, the application causes reddening, itching, a feeling of warmth or even of pain, and these symptoms are followed by dryness and in a few days by desquamation; afterwards, when the epithelium is shed, there remains a moist reddened surface. Where the concentration is still greater, blistering and ulceration are produced, with penetration to deeper tissues and inflammation of them. Repeated applications may cause great pain, and prolonged application causes destruction of the tissues. It is used, therefore, as an easily controlled counter-irritant to relieve deep-seated pain and influence inflammatory conditions.

On the mucous membrane of the mouth, dilute solutions produce a rather slighter effect than they do on the skin, owing to rapid removal by the alkaline secretion, but concentrated solutions affect mucous membranes as they do the skin. Iodine in solution in alcohol without potassium iodide is deposited on the gums, for instance, more readily than it is from the official solutions, in which the greater solubility of iodine in potassium iodide allows of its rapid removal.

In the stomach small quantities irritate it slightly and stimulate its functions, but larger quantities or prolonged application cause nausea and vomiting, and reaching the intestine may cause diarrhœa; and when large amounts have been administered or even when they have been injected into the circulation, the mucous membrane of the stomach and intestines have been observed to be inflamed, swollen and even marked with ecchymoses and hæmorrhages.

Absorption. — It is absorbed from the alimentary tract mainly as iodide, but also as iodate, partly also in combination with albumin. The general effects are similar to those following absorption of iodides, but there is a slight difference in the degree of the action. The skin appears to be affected less frequently, the thyreoid gland appears to be affected more easily and the train of symptoms known as "iodism" to be less frequently produced when iodine in small quantities is administered than when the iodides are given.

It is absorbed through the skin when applied locally, penetrates deeply, and causes absorption of tissues, osseous and cartilaginous material being rarefied and diminished. Pathological tissues, such as glandular enlargements and enlarged joints, are similarly affected, the probable cause of this being a leucocytosis similar to that produced by other counter-irritants but occurring to a greater degree.

Therapeutic Applications of the Halogens.—As disinfectants, chlorine and iodine are largely

employed, but bromine has practically ceased to be used.

Any solution containing one per cent. of uncombined chlorine may be used and is efficacious as a germicide when applied for an hour. When the gas is used there must be moisture present. The chlorinated solutions are even more efficacious and are generally employed to disinfect sewers, cesspools, fæcal or infected material, sputum, urine, etc. They must contain sufficient hypochlorite and 1 in 1800 should kill spores (B. anthracis) in two hours. An undue proportion of calcium chloride is not only useless but renders bleaching powder very deliquescent.

Chlorine is also used as a stimulating deodorising disinfectant for slowly healing offensive ulcers; and malignant sore-throats may be treated by gargles prepared by the decomposition of potassium chlorate (Liq. Chlori Compositus).

The disinfectant application of iodine is confined to tissues such as the skin, mucous membranes and teeth. Wounds and indolent ulcers may be treated with applications of the tincture repeated, or by single applications of the stronger liquor. Weak solutions (1 in 1500) have been employed with success in the treatment of chronic empyema. Pain and tenderness of the teeth, especially associated with retraction of the gums, are treated successfully either by washing with a 1 in 500 solution, afterwards removed by water, or by painting with a tincture without potassium iodide and leaving it in contact.

As a counter-irritant iodine is invaluable, and any degree may be produced. Thus swellings, enlarged joints, enlarged glands, and deep-seated pains and inflammations are frequently treated by the local application of the tincture or the ointment. Such are the painful joints of chronic rheumatism, and the slighter strumous glandular enlargements.

Iodides.—Iodine in combination with potassium and with sodium is most often used to produce the effects of iodine after absorption, and *Potassii Iodidum* and *Sodii Iodidum* are official. Iodide of ammonium has been used but is unstable; and iodide of starch is so easily broken up that it may be considered rather as a weak iodine, neither of these being official. Iodide of sulphur, a greyish-black solid, insoluble in water but soluble in sixty parts of glycerine, consisting of a mixture of sulphur and iodine partly in combination, may also be considered as a diluted preparation of iodine intended to produce its actions together with those of sulphur. It is not now official.

Potassium iodide is very soluble in water and in twelve parts of rectified spirit. It has a bitter pungent taste and feebly alkaline reaction.

Of it there is an official 10 per cent. *ointment* and a *liniment* of about the same strength, made with soap and glycerine.

Pharmacology.—It has no contact action on the skin, but has a very slight irritant action on mucous membranes and on raw surfaces, and large quantities in the stomach may cause nausea and vomiting. It is absorbed readily and excreted rapidly by the kidneys, the salivary, bronchial and other glands. The precise changes which it undergoes in the blood are still obscure, but the iodide is probably oxidised by the tissues resulting in the production of iodine, which then combines with proteins. This view is supported by the facts that hydriodic acid and free iodine have been detected in the stomach, and that irritation occurs in the respiratory passages, skin and other tissues, pointing to the presence of a product more irritating than potassium iodide itself; and additional evidence is provided by the increase of the iodine in the thyreoid gland after the administration of an iodide. Free iodine is not generally found in the tissues, but the ordinary starch reaction cannot detect by organic iodine compounds. That an iodide is decomposed in the body is observed during the administration of iodide of iron, iodine being excreted in the urine and iron in the fæces. Albuminates of the heavy metals form soluble compounds with iodides, and this fact is taken advantage of to aid their elimination.

The symptoms of irritation which sometimes occur during the administration of either soluble iodides, or even of free iodine, though less frequently, are grouped under the term *Iodism.* These symptoms include acute catarrh of the conjunctiva, and of the mucous membrane of the nose, frontal and maxillary sinuses, larynx and bronchi, and there may even be an œdematous condition. Severe headaches, lacrimation, profuse nasal discharge and bronchitis sometimes occur together with inflammation of the passages and increase of the secretions, notably the saliva. The usual time of occurrence of iodism is early in the administration, especially if large doses be given in concentration and if there is not free excretion in the urine. Small doses may produce these symptoms, but free dilution usually prevents their occurrence, as sometimes does the simultaneous administration of alkaline carbonates. There are other symptoms which, however, usually occur later, and are caused by irritation of the skin. Erythema, eczema, blisters, papules, pustules, crusts and hæmorrhages have all been observed to occur in varying degrees and to disappear when the administration was stopped. I have observed suppression of urine to occur during an acute attack of iodism, and albuminuria with other symptoms of irritation has occasionally been

met with, but the urine is generally increased in quantity when iodides are administered.

Among the toxic phenomena which iodides occasionally cause, those must not be overlooked which are referable to the stimulation of the thyreoid gland, an increase of its secretion and of its iodine content. These symptoms, resembling those caused by injection of thyreoid secretion in excess, include disorders of the nervous system characterised by localised pains or anæsthesia, tremors, headache, sleeplessness, etc., disorders of the circulation such as alterations in blood pressure with cardiac irregularity, rapidity and uneasiness; disorders of metabolism leading to emaciation; and glandular atrophy. These symptoms do not appear to be caused by iodine when the thyreoid gland is normal in size and function.

On the nervous and circulatory systems, with these exceptions, iodides have almost no action unless administered in very large quantities. Under these conditions, however, they weaken the central nervous system, resembling in action the bromides, and weaken the circulatory apparatus as do other potassium salts. On metabolism any action is slight, and, with the exception of producing a leucocytosis, there is little action on the blood. Anæmia, however, follows on the absorption of toxic amounts.

Potassium iodide is excreted mainly by the kidneys very rapidly, but also, though in small quantities, by all other glands. It is excreted mostly in the form of salts, some in organic combination, some as hydriodic acid (in the stomach) and a little free iodine. Three quarters of the amount administered is excreted within twenty-four hours and the remainder within a few days. It is not stored in the tissues for long (except in the thyreoid gland), but can be detected in most of them even in hair and muscles, in organic combination. It has not been found, however, in the brain. When it is being excreted by the bronchi it increases the amount and diminishes the viscidity of the secretion, and when by the skin it causes less irritation when the acid secretion is thoroughly removed by frequent washing.

Summary.—The actions of iodides, though obscure, depend on the activity of the iodine ion as toxic to organisms, to its irritant properties when set free during decomposition of the salt, to the salt action and to the stimulant action on the thyreoid gland and the supplying to it of a necessary constituent of the body.

Sodium iodide is official, and has the same actions as the potassium salt when given in doses not larger than those employed therapeutically, viz., from 5 gr. to 30 gr. Hydriodic acid is official in the forms of a 10 per cent. dilute acid and a Syrupus Acidi Hydriodici (1 per cent. of HI). It is used as a means of administering iodide, but has in addition acid characters. It is absorbed after neutralisation as alkaline iodides and produces the same effects as they do.

There are compounds of iodine recently introduced which have been recommended as possessing the action of the iodides without causing the occurrence of iodism. Some decompose very slightly, some more completely but slowly, and they, being eliminated slowly, give a more gradual effect than the rapidly absorbed and rapidly eliminated alkaline iodides. Such are the fatty compounds iodipin and sajodin, both of which, however, have been known to affect the thyreoid gland similarly to potassium iodide when all three were used in the same case (Schutz, *Wien. Med. Woch.*, 1908). About 40 gr. of the former, injected twice, caused symptoms of thyreoiditis, and so also did 7½ gr. of the latter thrice repeated administered by the mouth, these being the usual doses.

Therapeutic Applications of Iodides.—These depend on the stimulation of absorptive processes, the effects on secretions, and the ease of elimination. Iodides are largely prescribed, therefore, in cases of tertiary syphilis with gummata or other swellings and in scrofula with enlarged glands; also in rheumatic and gouty conditions. In respiratory diseases, such as bronchitis, where the secretion is scanty and tenacious, the amount of the secretion is increased and it becomes more fluid. In bronchitic asthma, croup and diphtheria they are also used. In the treatment of goitre the iodides benefit by influencing the thyreoid secretion, and they are valuable in the treatment of aneurysms, though the explanation of their value is obscure. To aid elimination of metallic poisons, such as mercury or lead, iodides are often administered because of the solubility of the organic metallic compounds in them.

Iodoform, CHI_3, occurs in unctuous yellow glistening crystals, or powder, with a characteristic, penetrating and persistent odour which is disagreeable, as is also the taste. It is practically insoluble in water, but dissolves in five parts of ether, and in ten parts of boiling rectified spirit and in eighty parts of cold. It dissolves in fixed oils and volatilises when heated. A 10 per cent. ointment is official, and there is a suppository containing 3 gr. (0·2 gramme) in each.

Pharmacology. — It has no action on the unbroken skin, but can be absorbed from it owing to its solubility in fats. Oxidation of it causes liberation of its iodine, and this may take place to a slight degree on raw surfaces. It is feebly toxic to micro-organisms, much less so than was thought to be the case when it was first used, and its usefulness as a local application to septic sores must be explained by its exerting a combination of actions,

each slight in itself but productive of a cumulative effect, rendering it efficient for this purpose. It diminishes the activity of micro-organisms, and it also slightly delays inflammatory action, preventing leucocytes from migrating rapidly. It diminishes secretion locally so that wounds become drier, which condition also is inimical to growth of organisms, and it forms an adhesive protective layer which prevents their spreading. The finer the division of the powder the more efficacious is it, but it may produce irritation because of its being more readily decomposed.

On mucous membranes and on raw surfaces it causes a slight diminution of sensitiveness and is much less irritating than is iodine. After local applications of iodoform to the rectum, the sensations caused by the passage of fæces may not be felt, and it is slightly sedative to the stomach. After absorption, which may take place from a large wound in sufficient amounts to cause toxic effects, some of it is decomposed by alkalies and by the proteins forming iodides and protein compounds, while some is unchanged, and these products are excreted as has been already described. This change takes place slowly, and iodides, therefore, are found in the urine for a considerable period of time, though iodides are excreted rapidly from the blood, an indication of the storage of the substance in the tissues and its gradual decomposition.

The symptoms caused by it are, therefore, those caused by unchanged iodoform, which exerts an action mainly on the nervous system, as well as those transient and slight effects on secretions and skin due to the iodine and iodides, and lastly those nervous and circulatory disturbances which occur on account of the disturbance of the thyreoid gland.

The action of iodoform on the brain is obscure, but is characterised by the occurrence of headache, nausea and vomiting when small amounts have been absorbed. Larger amounts cause sleeplessness, mental depression, restlessness and anxiety. This condition is progressive, becoming more profound, depression developing into melancholia, and even into suicidal mania with hallucinations of persecution, and may afterwards become one of permanent insanity, or it may be succeeded by delirium and death or by progressive stupor and collapse. The presence of iodoform in the salivary and nasal secretion even in small amounts cause a persistent disagreeable smell and taste. There may be albuminuria. Slight symptoms of iodism may be met with due to iodine and iodides. Cardiac acceleration and rise of temperature, with increase of thyreoid secretion, are probably to be referred to effect on the gland.

Post-mortem changes are either of an inflammatory nature in the alimentary tract, like those met with in iodine poisoning, or more or less extensive fatty degenerative changes in the tissues, more closely resembling those met with in poisoning by alcohol and chloroform. It is, therefore, of interest to observe that the action of iodoform on the nervous system differs from that exerted by iodides and rather approximates to that exerted by derivatives of methane; but on the other hand there is little narcosis and no general anæsthesia; either of which might have been expected to be produced by a substance of its composition.

Its odour being so objectionable, other substances without this characteristic, but possessing the main advantages of iodoform for local application, have been sought. Such are combinations of iodine with derivatives of quinoline, phenyl and pyrrhol, which, it was hoped, would show an intensification of the germicidal properties. Examples of these are known as loretin, aristol and iodol, the two last being official in the United States. The last-named undergoes some decomposition in the body, but this has, however, not been observed when the others are administered. They have not the odour of iodoform, are as insoluble and not conspicuously superior in germicidal power.

Therapeutic Applications of Iodoform.—These are to bring about disinfection and rapid healing of wounds, sores and ulcers. The powder itself in a finely divided form is the most efficacious and the most often employed. Its local anæsthetic action is also made use of in painful conditions of the rectum associated with sores or wounds and the suppository is largely used for this purpose.

Bromides.—The official bromides are those of *potassium*, *sodium* and *ammonium*, occurring in colourless cubical crystals, soluble in two parts of water and less soluble in rectified spirit, sodium bromide 1 in 16, while the potassium salt requires 200 parts to dissolve it. They are decomposed less easily than the iodides, but undergo similar changes, and are excreted less rapidly.

Pharmacology.—Potassium bromide in dilution is very slightly irritating, even to mucous membranes, but in concentration irritates and may even exert a caustic action on weak tissues. When in contact with muscular and nervous tissues it depresses them, acting in these respects like many other salts. When taken internally irritation of the alimentary tract may be produced, with disturbance of digestion when the solution is concentrated. It is readily absorbed when given in quantities of from five to thirty grains, and exerts its action chiefly on the nervous system.

A train of symptoms known as *Bromism* may occur if larger quantities are administered or if these quantities are given for a prolonged

period, which symptoms are caused by irritation during excretion. A catarrhal condition of the respiratory passages occurs, a tenacious mucus accumulates and is expectorated with difficulty, the breath is offensive and the mucous membrane of the nose and throat is swollen. The skin is also irritated, the usual appearance being that of a papular or pustular eruption, though other forms of irritation are met with, the occurrence of boils not being uncommon, and sometimes there may be merely a discoloration of an erythematous type. The symptoms of bromism are less frequent in occurrence and less severe in character than those of iodism, doubtless owing to the greater stability of the bromide salt, the catarrhal symptoms especially being very much less frequent. When the administration is long continued, there may follow mental depression, impairment of cerebral functions, loss of memory, hebetude, impairment of motor functions and dullness.

Apart from the salt action and the irritative phenomena the action of small quantities is to depress the nervous system without previously exciting it. In cold-blooded animals slight depression of the brain is observed to occur, voluntary movements being diminished; but a much more conspicuous effect is exerted on the spinal medulla, the activity of the reflex mechanism being progressively diminished until it is entirely lost. The motor conductivity of the spinal medulla is subsequently paralysed if the dose is large enough, and finally the peripheral nerves cease to respond to stimulation.

On warm-blooded animals, cerebral and cerebellar symptoms are rather more prominent, stupor and imperfectly co-ordinated movements having been observed and sometimes paralysis of the respiratory centre in the medulla. The cerebral cortex also is rendered much less sensitive to irritation, and in them also diminution of reflex excitability is observed to occur. On man the effect on the brain is still stronger in proportion, mental activity being impaired, the power of memory diminished or even lost when large doses are taken, and drowsiness followed by sleep is produced by comparatively small quantities. The reflex mechanism is also depressed, certain characteristic reflexes being sometimes completely abolished, such as the reflex obtained by touching the fauces, that from the bladder, and even the sexual reflexes. Still larger quantities depress the conductivity of the afferent nerves and sensation is diminished. These latter actions help in no small degree to bring about the tendency to sleep by preventing the usual stimuli from reaching the brain. The depression of the spinal medulla is even more clearly seen when the bromide is administered in conditions of increased reflex excitability, whether caused by disease or by the action of such an excitant as strychnine. Bromides do not depress the circulation except in very large doses, and though the temperature may fall, this is secondary to the diminished muscular activity; and any action on the glandular structures is slight as compared with that excited by iodides.

Bromide of potassium is excreted largely by the kidneys, though somewhat slowly, and in other secretions to a less extent. The chlorine in normal secretions is to some extent replaced by bromine, and a considerable replacement of hydrochloric acid by hydrobromic acid has been observed in the stomach after continued administrations, and a little free bromine has been observed in some secretions. Metallic albuminates are as soluble in bromide of potassium solutions as, if not more so than, in those of iodides, and may therefore be eliminated from the body by this means.

Post-mortem examination after continued administration or, in some cases, after a few large doses, shows degenerative changes in the nerve cells, alteration both in their reaction to chemical agents and in their microscopic characters.

In addition to possible degenerative changes it must be observed that successive doses of bromides may for a time cause increasing effects owing to the slow excretion, only one-tenth of the dose being excreted during the first day. The proportion excreted, however, rises until nearly the whole amount ingested is eliminated in a short time, the cumulative effects then ceasing to be manifested. A further point to be mentioned is that the bromide can be rapidly displaced from the tissues by the administration of chlorides.

There is little need to discriminate between the actions of the potassium salt on the one hand and those of sodium and ammonium on the other. The actions of the basic ions no doubt differ, but the quantities usually administered are too small to elicit the difference. The sodium salt is described as less depressant by patients who have taken it subsequently to a course of potassium bromide, but suggestion as to the probability of this effect being observed possibly plays the larger part in producing this impression.

Dilute hydrobromic acid is a weak solution which combines the acid action with those of a bromide. Its acid character prevents its being administered in as large amounts with as little irritation as the alkaline salts.

Therapeutic Applications of Bromides.—In all forms of cerebral excitement not associated with inflammatory changes bromides are used, but especially in those cases associated with motor-disturbances such as epilepsy. To soothe the

nervous irritability following on mental worry, overwork, neurasthenia; to allay excessive vomiting whether cerebral or reflex; and to diminish the spasms in strychnine poisoning and tetanus, bromides are very useful. In infantile convulsions, nocturnal incontinence of urine, night terrors in children, nymphomania or any other condition of reflex irritability they are administered with great benefit. In these cases they cause sleep and alleviation of the symptoms. They sometimes diminish neuralgic pains and migraine, and they have been employed in the treatment of exophthalmic goitre and to aid in the elimination of metallic poisons.

Fluorides.—These are extremely irritating salts, much more so than those which we have been considering, and more powerful as poisons to micro-organisms and protoplasmic tissues. Absorbed very slowly and forming insoluble calcium salts, they exert their main action on the alimentary tract, and the small amount absorbed hinders the coagulation of the blood.

Preparations of Halogens and Haloids

Calx Chlorinata.				
Liquor Calcis Chlorinatæ	B.P. and U.S.P.			
Liquor Sodæ Chlorinatæ				
Liquor Chlori Compositus.	U.S.P.			
Gargarisma Chlori.	B.P.C.			
Iodum.				
Tinctura Iodi Mitis	B.P.	2½ per cent.	Dose, 2–5 min.	12–30 cm.
Tinctura Iodi Fortis		10 per cent.		
Tinctura Iodi		7 per cent.	1–2 min.	5–10 cm.
Liquor Iodi Compositus	U.S.P.	5 per cent.	1–3 min.	6–18 cm.
Unguentum Iodi.	B.P. and U.S.P.	4 per cent.		
Sulphuris Iodidum.	U.S.P.			
Potassi Iodidum	B.P. and		Dose, 5–20 gr.	3–12 dm.
Sodii Iodidum	U.S.P.		5–20 gr.	3–12 dm.
Unguentum Potassii Iodidi				
Linimentum Potassii Iodidi.	B.P.			
Acidum Hydriodicum dilutum.			5–10 min.	3–6 dm.
Syrupus Acidi Hydriodici.			½–1 dr.	2–4 mils.
Iodoformum	B.P. and U.S.P.			
Unguentum Iodoformi				
Suppositoria Iodiformi.	B.P.			
Thymolis Iodidum ("Aristol")	U.S.P.		1–4 gr.	6–25 cg.
Iodolum			1–4 gr.	6–25 cg.
Potassii Bromidum			5–30 gr.	3–20 dg.
Sodii Bromidum			5–30 gr.	3–20 dg.
Ammonii Bromidum	B.P. and U.S.P.		5–30 gr.	3–20 dg.
Acidum Hydrobromicum Dilutum			15–60 min.	1–4 mils.

W. C. S.

THE PHARMACOLOGICAL ACTION OF SODIUM, POTASSIUM, CALCIUM, LITHIUM, AMMONIUM AND MAGNESIUM

Sodium, potassium and calcium are indispensable to the life of every animal cell. A supply of these salts is essential to the growth of cells, and their presence in certain concentrations in the fluids around them is necessary to maintain the life of the cells. The physiological functions of these ions may be divided into (1) their physical action, which they possess in common with many other salts, (2) their function as essential constituents of all cells, and (3) the specific action of these ions when present in circulating fluids upon the activities of the cells. These physiological functions are so important that it is necessary to consider them before proceeding to discuss the importance of ions in normal metabolism and their action in disease.

A salt such as NaCl when dissolved in water dissociates into a positive ion or kation (Na), and a negative ion or anion (Cl), and most of the actions of salts upon living tissues are produced by the dissociated ions. The present paper is concerned with the action of the kations, and the anions are dealt with elsewhere.

The chief physical action that all salts have in common is the production of osmotic pressure; this is discussed elsewhere, but it may be mentioned that the chief action of NaCl, either in the body or in artificial perfusion fluids, is that of maintaining the osmotic pressure; and no other salt can be substituted for it in mammalian tissues, for all other salts, in concentrations high enough to maintain the osmotic pressure, exert injurious specific effects.

There are several other general physical properties of kations of great physiological importance, such as the power to precipitate colloids, and especially proteins, and the power of colloids to absorb different kations: the relation between these properties and the physiological action of the kations is, however, too complicated to be considered here.

Distribution of Na, K, and Ca, in the Tissues.—Analyses show that the three substances Na, K and Ca occur in all the tissues and fluids of the body, and a supply of these bodies is essential to the growth of the organism, but while Na and K are fairly evenly distributed in the body, no less than 99 per cent. of the Ca is contained in the skeleton. Analyses of entire organs do not show any very well-marked differences in the distribution of Na and K, but a comparison of the amounts of these salts contained respectively in the cells and in the plasma surrounding the cells, yields interesting results.

Table I.—Salt Content of Tissues per Cent.

Tissue.	Animal.	Observer.	Sodium.	Potassium.	Calcium.
Muscle cells .	Frog	Urano	0·008	0·195	0·010
Blood plasma	,,	,	0·246	0·018	0·009
Red blood corpuscles	Dog	Abderhalden	0·282	0·023	0·010
Serum . . .	,,	,,	0·426	0·023	0·010
Red blood corpuscles	Rabbit	,,	0·000	0·523	0·000
Serum . . .	,,	,,	0·440	0·026	0·010

These figures show that in all cases there is a marked difference in the concentrations of the inorganic salts in the cells and in the fluids surrounding the cells, the cells containing less sodium and usually more potassium than the

fluid, the difference being best marked in the case of the rabbit's blood corpuscles.

Specific Action of Na, K, and Ca upon Cells.—The comparative analyses of cells and plasma show that different concentrations of Na and K are maintained outside and inside the cells, and this confirms the view already stated that Na, K and Ca do not penetrate living cells. Each of these ions, however, by its action upon the surface of the cell, produces a specific effect upon the activity of the cell.

Isolated tissues can only continue to live in isotonic fluids, and moreover the fluids must be faintly alkaline. Furthermore, Ringer showed that the isolated frog's heart could maintain its activity only when perfused with a fluid containing all three salts, Na, K, and Ca, that there was an optimum proportion of the three salts, that any variation in this proportion produced definite changes in the heart's activity, and that any marked changes killed the heart.

The formulæ for Ringer's fluid vary, but the following have been found to give satisfactory results—

(1) For the frog's tissues—

NaCl . .	0·65	per cent.
KCl . .	0·014	,,
$CaCl_2$.	0·012	,,
$NaHCO_3$	0·01	,,
Na_2HPO_4	0·001	,,

(2) For mammalian tissues—

NaCl . .	0·8	per cent.
KCl . .	0·03	,,
$CaCl_2$.	0·02	,,
$NaHCO_3$	0·02	,,
Glucose .	0·2	,,

Other workers have confirmed Ringer's conclusions, and the same laws appear to hold good for all other tissues of the body, a fluid containing a certain proportion of these three ions, Na, K, and Ca, being essential for the maintenance of the life of the isolated tissues; moreover, it has been shown that the action of two ions, Na and K, antagonise that of Ca, and that the first condition for maintaining the life of the tissue is to maintain a certain balance between the concentrations of Na and K on the one side and of Ca on the other.

Loeb has shown that a similar balance of salts is necessary for the life of numerous marine and fresh-water organisms. His researches upon *Fundulus heteroclitus* are of special interest; this marine fish possessed a truly wonderful power of adaptability, for it lived equally well in sea-water, fresh-water, or distilled water, or even in sea-water to which a large excess of NaCl (5 per cent.) had been added. When, however, the fish was put into distilled water containing 3·6 per cent. NaCl, it died in ten hours, but this poisonous action of pure NaCl was abolished by the addition of $CaCl_2$ 0·07 per cent. and KCl 0·046 per cent.

Loeb and his pupils have experimented upon a long series of organisms, and his experiments upon the influence of salts in determining the development of sea-urchin's eggs are well known. Different organisms showed different powers of resistance to changes in the inorganic constituents of their environment, but in all cases the presence of any one ion alone produced a definite toxic effect, and this toxic action was antagonised by the addition of a second salt, and in most cases the presence of the three salts, Na, K, and Ca, was more favourable than that of only two ions.

Similar results have been obtained with plants, for it was early shown that plants could grow only when supplied with certain salts. Osterhout has shown recently that laminaria is killed by pure solutions of either Na or Ca, but that it will survive in a mixture of these two salts. All these results agree in showing that a pure solution of any kation exerts a poisonous action upon living tissues, and that in order to maintain life a certain balance must be maintained between the three kations, Na, K and Ca, and that there is a specially marked antagonism between the monovalent kations (Na and K) and the divalent kations (Ca).

Intact organisms, animals or plants, possess a much greater power of resistance to changes in the salt content of their environment than do isolated tissues, and these last are markedly affected by slight changes, and rapidly killed by any extensive changes in their environment.

The researches of Carrel upon the survival and growth of isolated tissues have led him to the conclusion that "the growth of the tissues of mammals is probably controlled by the conditions of the interstitial lymph, in the same way that the growth of the egg of the sea-urchin is influenced by the conditions of the water."

The Metabolism in Intact Mammals of Na, K, and Ca.—Forster showed that dogs, if fed upon an ash-free diet, died as quickly as if deprived of all food, and these experiments have been repeated and confirmed by Lunin, who experimented upon mice. Other workers have determined the effects of depriving animals of one of these kations, or of adding a great excess of one of them.

Voit and many subsequent observers showed that deprivation of Ca produced marked effects upon the bones. Puppies deprived of calcium, formed bones more fragile and flexible than normal, whilst in adult dogs the bones did not lose in strength but became considerably lighter and more porous.

Luithlen fed rabbits upon a diet containing

a large excess of potassium, and found that with such a diet there was a loss of calcium and that the animals suffered in health. From these and other experiments he concluded that the bad effects of over-mineralisation or demineralisation were not due so much to the actual excess or deficit in the food, as they were to the upsetting of the balance in the body tissues between the various ions.

Earlier workers showed that an excess of any one kation in the food caused not only an increase in the amount of this kation excreted in the urine, but also an excess in the amount of the other kations excreted, thus producing a loss to the body of the other kations. Bunge pointed out that this "washing out" effect was of importance to people living on a vegetarian diet, for these take in a great excess of potassium and suffer from loss of sodium, unless excess of sodium is added to their diet in the form of common salt.

The Metabolism of Inorganic Salts in Infancy.—During the first year of its life the infant requires large quantities of inorganic salts to build up its tissues; it is therefore of highest importance that the infant's food should contain a sufficient quantity of salts, and during recent years the inorganic metabolism of infants has been studied very carefully in connection with the question of the artificial feeding of infants.

Söldner analysed the bodies of breast-fed infants and concluded that no less than 50 per cent. of all the inorganic salts taken in the food were utilised to form the body tissues; of the different salts in the food 11 per cent. of K, 35 per cent. of Na, and 65 per cent. of Ca were utilised to build up body tissues. It is apparent that there is a very narrow margin between the quantity of Ca supplied and the minimal amount required by the infant.

Cow's milk contains more inorganic salts than human milk, as is shown by the following table.

Salts in milk (in grams per litre)—

	Human milk	*Cow's milk*
Na_2O . .	·35	0·5
K_2O . .	·88	1·7
CaO . .	·37	1·9

This difference between the salt content of the two milks is, however, compensated for by the salts of cow's milk being less completely absorbed, and being retained in the body in a much lower percentage.

Blauberg estimated what percentage of the salts taken in the food was retained by the body in infants, and found that the retention of sodium and potassium was nearly the same with cow's milk as with human milk, but that whereas 76 per cent. of the calcium of human milk was retained, only 22 per cent. of that of cow's milk was retained. Deficient calcium in the food produces in young animals deficient bone formation, and therefore many workers have tried to establish a relation between deficient calcium absorption and rickets, but there is no evidence that the two are associated. Schabad has shown that the early stages of rickets are associated with a negative calcium balance (*i. e.*, more calcium is excreted than is taken in the food), but he found that rickets occurred in cases of breast-fed children in which the milk contained larger quantities of calcium than normal (in one case the mother's milk contained 0·88 gram Ca per litre).

Action of Excess of Salts on Infants.—There is a considerable amount of evidence that any great alteration in the relative amounts of Na, K, and Ca taken in the food is injurious to infants. Meyer and Cohn attempted to improve the nutrition of bottle-fed babies about three months old by adding excess of Na, K, and Ca to their food. They showed that excess of NaCl (4 grams per diem) produced a great increase in weight which was due to retention of sodium, and a consequent retention of water; this is due to the infant's kidneys being incapable of excreting rapidly large quantities of sodium. Excess of sodium chloride produces no such effect in healthy persons, but Widal and Javal showed that similar effects to the above were produced when sodium chloride was given to adult patients suffering from nephritis. Excess of potassium had but little effect on the weight of infants, but excess of calcium produced a rapid fall in weight. The last effect, however, may have been due to the calcium hindering absorption from the alimentary canal. Excess of sodium in the food produced a well-marked rise in temperature, and excess of potassium sometimes produced the same effect, but excess of calcium produced a fall in temperature.

These results show that alterations in the salt content of the food produce injurious effects in infants that are not produced in healthy persons. It is also interesting to observe the opposite effects produced by excess of sodium and calcium.

Hume made similar observations to those of Meyer, but found that the quantity of sodium chloride required to produce an increase in weight in a normal infant was so great as to make the food highly unpalatable. It is doubtful, therefore, whether such variations in the salt content of the food as occur in artificial feeding are of any practical importance.

Pharmacological Action of Sodium

Ringer showed that presence of sodium was essential to the maintenence of the life of an excised tissue, and he showed that sodium acted as a depressant to the heart and that its action was antagonised by calcium.

Loeb found that striped muscle gave spontaneous twitches in isotonic sodium chloride, and that these twitches were abolished by calcium, but the significance of this observation is not clear.

The general salt-action of sodium chloride has been mentioned already. The chief action of sodium chloride is undoubtedly the physical one of maintaining the osmotic pressure, but the salt also exerts a definite specific action on the body, and isotonic sodium chloride cannot be regarded as a normal or indifferent fluid when injected into the body.

Therapeutic Action of Sodium

The action of excess of Na upon infants has been mentioned, but excess of Na appears to have little action upon healthy adults. Widal and Javal showed that in patients suffering from nephritis with œdema, an excess of NaCl in the food increased the œdema, and a diminution of NaCl reduced it. This effect is explained by the earlier observations of Strauss, who showed that kidneys in nephritis could not excrete NaCl rapidly, and that there was considerable retention of NaCl in a patient even when taking a normal diet. Any excess of NaCl is excreted rapidly by a normal person, but in an infant or a nephritic the kidneys cannot excrete the NaCl rapidly and the retention produces œdema.

Clinical observations as to the effect of a sodium—chloride—free diet upon œdema in nephritis have in many cases yielded favourable results.

Action of Injections of Physiological Saline.—In recent years large injections of salt solutions, intravenous, subcutaneous or rectal, have been employed with increasing frequency.

A large number of workers described a rise of temperature following intravenous injection of NaCl, and some observers (Meyer and Rietschel) stated that this rise was prevented by addition of calcium to the saline solution. Penfold and Hort have shown, however, that the rise of temperature is due to the presence of a poisonous substance that appears when distilled water is kept many days, and that this substance probably is a product of bacterial disintegration; these results have been confirmed by other workers.

Sodium chloride, therefore, is not the chief cause of the so-called "salt-fever" that follows injection of isotonic saline, but there is some evidence that such fever is decreased by addition of calcium to the fluid. Injections of sodium chloride undoubtedly produce glycosuria, and Fischer states that this glycosuria is stopped by the administration of calcium.

Joseph and Meltzer studied the effects of injections of hypertonic solutions of NaCl, KCl, $CaCl_2$ and $MgCl_2$ into dogs, and found the minimum lethal doses per kilo to be: NaCl, 3·9 gram; KCl, 0·68 gram; $CaCl_2$, 0·44 gram; $MgCl_2$ 0·22 gram. These authors conclude that although sodium is much less toxic than the other salts, nevertheless it produces certain specific effects, namely, twitching of muscles, convulsions, and finally paralysis of respiration and heart failure. Evans has collected several cases in which collapse or death in patients appeared to be due to excess of sodium administered.

These results all suggest that excess of sodium chloride cannot be injected with impunity into the body, nor even given per rectum in the case of a patient whose kidneys are not functioning in a normal manner, as in the case of a patient suffering from shock. Since many of the undesirable effects of sodium are antagonised by calcium, the addition of calcium to saline solution is desirable, and this may be done by using tap water, which in London contains 0·01 per cent. calcium. Solutions for intravenous injections should be made either of tap water, or of freshly distilled water, or of distilled water that has been kept since distillation under the strictest aseptic conditions (cf. Penfold and Hort); the fluid should be isotonic with mammalian blood and contain 0·9 per cent. NaCl, and the addition of 0·01 per cent. $CaCl_2$ appears advisable. It may be mentioned that a teaspoonful of sodium chloride in a pint of water makes a solution the strength of which may vary between 0·5 per cent. and 1·4 per cent.; since it appears from the work of Dale that slight alterations in osmotic pressure can produce very marked changes in the mammalian tissues, it is obvious that careless preparation of fluid for intravenous injection is dangerous.

Rogers has used intravenous injections of hypertonic solutions (NaCl, 1·3 per cent.; $CaCl_2$, 0·04 per cent.; KCl, 0·07 per cent.), and has obtained excellent results both in cholera and in infantile diarrhœa, for the solution was found to be excreted into the gut much more slowly than normal saline. The Quinton sea-water treatment of infantile diarrhœa may also be mentioned. This treatment consists in injecting sterile sea-water which has been diluted two and a half times with distilled water. The composition of this diluted fluid is about as follows: NaCl, 1·1 per cent.; KCl, 0·03 per cent.; $CaSO_4$, 0·058 per cent.; Mg salts, 0·24 per cent.; the composition of the fluid is strikingly similar to that recommended by Rogers, and there appears some evidence that it produces better results in the treatment of diarrhœa than the injection of normal saline. Sutherland and McKay recommend a very similar solution (*i. e.* hypertonic NaCl with a little $CaCl_2$) for injection in blackwater fever, for they state that such a solution inhibits hæmolysis.

Pharmacological Action of Potassium

Potassium has a very marked depressant action upon excised tissues, and a small increase in the amount of potassium in Ringer's solution depresses the activity of the isolated heart of the frog or the mammal; this effect, however, is antagonised by calcium, and within certain limits the action of excess of potassium upon isolated tissues is abolished by the addition of excess of calcium. If potassium is injected into an intact animal, it produces well-marked depression of the central nervous system, which causes muscular weakness and failure of respiration; finally the heart muscle is directly affected, the blood pressure falls rapidly and death ensues. Joseph and Meltzer show, however, that the action of potassium upon the heart in the intact animal is much less marked than is its action upon the excised heart.

Potassium given in excess by the mouth produces no direct poisonous effect, for with a vegetable diet as much as 50–100 g. ($1\frac{1}{2}$–3 oz.) of potash are taken daily (Bunge). The reason for this immunity is that potassium is excreted as rapidly as it is absorbed; but Bunge showed that potassium may produce an indirect effect by "washing out" sodium from the body.

Pharmacological Action of Calcium

Metabolism.—Calcium is absorbed from the small intestine, and about 10 per cent. of the amount absorbed is excreted in the urine and the remainder excreted in the fæces. The absorption of calcium is diminished by the presence of excess of alkali or fat, or the presence of any anion with which calcium forms an insoluble salt.

Action on Ferments.—The presence of calcium is necessary for the occurrence of many ferment actions, *e. g.*, the clotting of blood by fibrin ferment, the clotting of milk by rennet, and the action of trypsin upon peptones.

Action on Muscles and Nerves.—The presence of calcium is necessary for the life of the excised hearts of frogs or mammals, and if deprived of calcium the heart dies in diastole; excess of calcium on the other hand causes increased contraction and diminished diastolic relaxation. Excised striped muscle, if deprived of calcium, shows spontaneous muscular twitchings and paralysis of the motor nerve-endings, but a trace of calcium abolishes both of these effects.

Action on Central Nervous System.—Roncoroni found that diminution in calcium produced epileptiform convulsions, and that an excess of calcium diminished the excitability of the brain.

MacCallum and Voightlin produced tetany by removal of the parathyreoids, and stated that injection of calcium produced temporary arrest of the tetany. Other workers also agree that excess of calcium produces a feeble, depressant action on the central nervous system. On the other hand the anæsthesia produced by injection of magnesium is inhibited by calcium, but the reason for this effect is unknown.

Action on Secretion.—L. Loeb produced œdema in rabbits by injecting excess of sodium chloride solution. He found that calcium diminished the secretion of fluid by the kidneys, and into the alimentary canal, but rather increased the amount of ascitic fluid.

Chairi and Januschke stated that calcium inhibited the formation of inflammatory effusions. They found that injection of calcium inhibited mustard oil from producing œdema when applied to the conjunctiva, and prevented the formation of pleural effusions which normally followed the administration of thiosinamine or sodium iodide. Levy, however, found that calcium did not prevent the formation of hydrothorax in guinea-pigs after administration of diphtheria toxin.

Therapeutic Action of Calcium

Calcium has been administered for an enormous variety of different conditions, but in general the evidence is very unsatisfactory, and a definite therapeutic action has been shown in only a very few cases.

Action on Blood Coagulation. — Coagulation of the blood cannot occur in the absence of calcium, but excess of calcium *in vitro* does not hasten the occurrence of blood coagulation. Wright and a number of other workers found that administration of calcium by the mouth increased the rate of coagulation, both in health and in those diseases in which this rate is abnormally slow. Other very careful workers have obtained completely negative results, and recent work suggests that the experimental error is far too great to allow of reliable results being obtained by any of the present methods. Addis showed that very slight variations in room temperature might produce a large experimental error, Von den Velden has shown that all sorts of local reflexes alter the coagulability of the blood 50–100 per cent. and that these effects last 10–60 minutes: such reflexes are application of heat or cold to any part of the body, administration of astringents by mouth or inhalation of turpentine. In connection with this work it may be noted that several observers agree that excess of calcium given by the mouth increases the quantity of calcium in the blood, but evidence is lacking that the diseases in which there is deficient coagulability of the blood are associated with a deficiency of calcium in the blood.

Action on Central Nervous System.—Calcium has been recommended in the treatment of infantile tetany, asthma, epilepsy and exophthalmic goitre. There is some evidence that excess of calcium produces a depressant effect upon

the central nervous system, but little evidence that its administration is of value in any of the above-mentioned diseases.

Action on Serum Diseases.—Wright showed that administration of calcium prevented serum disease, chilblains and urticaria. This has been confirmed by Gewin, who observed the effects of antitoxic serum upon 200 cases, of which 100 were treated with calcium. Of the 100 thus treated only four had serum disease associated with a rise of temperature and a general eruption, but of the 100 cases not given calcium, twenty-three showed these symptoms.

Other Actions of Calcium.—Wright states that calcium inhibits physiological albuminuria, but other workers have not confirmed this conclusion.

Calcium metabolism is closely associated with the internal secretion of the ovaries, and removal of the ovaries produces a diminution in the excretion of calcium. Several observers have tried to show that an alteration in the calcium metabolism is associated with many of the disorders of menstruation and also of pregnancy, and that these diseases are improved by administration of calcium, but the evidence is very imperfect. Osteomalacia is associated with an enormous loss of calcium from the body, but excess of calcium in the food produces no benefit. The disease, however, is cured by castration or ovariotomy. Calcium excretion is decreased by removal of the thyreoid gland and increased by administration of thyreoid extract. It is evident that there is a close connection between calcium metabolism and several of the ductless glands, but the significance of this relation is unknown.

Lithium

Lithium exerts a feeble potassium-like action on excised tissues. In large doses it is poisonous, whether given by the mouth or subcutaneously, and causes nausea, vomiting and diarrhœa, and in particular produces a specific acute gastro-enteritis which is followed by emaciation weakness and death from collapse. Lithium is absorbed rapidly from the stomach and is excreted principally in the urine but also by the fæces. It appears in the urine fifteen minutes after the time of its administration. Lithium produces diuresis in exactly the same manner as sodium salts, by its salt action, but it has no specific diuretic effect.

In 1841 Lipowitz found that lithium urate was very soluble, and ever since lithium has been used in therapeutics as a solvent for uric acid. This use is wholly irrational, for lithium urate could only be formed in an alkaline urine, and with a concentration of lithium far higher than that sufficient to kill the patient. In moderate doses lithium is useless, and in larger doses dangerous.

Mineral Waters

The action of mineral waters cannot suitably be discussed here. Albu and Neuberg furnish analyses of 150 such waters, but no definite relation can be discerned between the varying compositions of the waters and their varying claims to heal diseases. It is a matter of general experience that waters drunk at home do not produce the same effects as when taken at a spa, and undoubtedly most of the beneficial effects observed are due to improved hygienic conditions.

Ammonium

This ion differs from Na, K, and Li in that it is far more toxic, for it has a specific stimulating action upon the central nervous system.

Action on Muscle and Nerve. — Ammonium hydrate rapidly penetrates living cells even in very weak solutions, although sodium and potassium hydrate in similar concentration do not penetrate the cells. Ammonium therefore acts as a poison to isolated tissues, protozoa or eggs of marine animals. In small doses ammonium acts on striped muscle in a manner similar to potassium; it produces paralysis of the motor nerve-endings.

Action on Central Nervous System.—Ammonia salts, when injected into a frog, produce increased reflexes and convulsions. These can be shown to be due to a strychnine-like action upon the spinal cord.

In a mammal similar convulsions follow the injection of ammonia; moreover, the medullary centres are stimulated, and acceleration of respiration, slowing of the heart, and rise of blood pressure occur.

Secretions.—Ammonia gas irritates the nasal mucous membrane and produces in this way a series of reflexes such as sneezing and coughing. Ammonium vapour is inhaled in fainting in order to stimulate the medulla oblongata reflexly in this manner. Ammonium salts irritate the stomach and thus act as carminatives and emetics; they act as expectorants by producing as a reflex an increase in the bronchial secretion. After absorption ammonium directly stimulates the medulla and thus increases the bronchial secretion by stimulation of the vagus nerve.

Excretion. — Ammonium carbonate is converted by the liver into urea and excreted in the urine. Since ammonium salts are converted into urea in this manner, they do not make the urine less acid.

Magnesium

Magnesium occurs with calcium in all the tissues of the body, but unlike calcium its presence is not necessary for the survival of an isolated organ.

Magnesium is absorbed in small quantities from the small intestine, and most of it is

excreted in the urine. When a salt of magnesium is injected intravenously in a mammal it rapidly produces anæsthesia, and in larger quantities produces first arrest of respiration, and finally death from heart failure; it is twice as toxic as calcium.

Meltzer showed that the depressant action of magnesium upon the central nervous system is inhibited in a remarkable manner by injection of calcium, but no explanation has been given for the remarkable antagonism.

This depressant action of magnesium has been utilised to control the convulsions of tetanus. The magnesium is injected subdurally and completely inhibits the convulsions; its action, however, is due to its general anæsthetic properties and not to any specific curative effect.

When taken by the mouth salts of magnesium are absorbed very slowly and therefore have a well-marked cathartic action. This action is discussed elsewhere (*Saline Purgatives*).

Magnesium sulphate injected subcutaneously slightly increases peristalsis and so may produce purgation. There is no evidence that the purgation produced when the drug is given by the mouth is due to any action of the drug after absorption.

Preparations

Sodium.

1. Sodii Chloridum (B.P., U.S.P.). 10–240 gr. (½–16 g.).
   (*a*) Liquor Sodii Chloridi (B.P.C.). Physiological or Normal Saline Solution. Sodium Chloride 0·91 per cent. in distilled water. It is used for subcutaneous, intravenous and rectal injections. Ringer's fluid (cf. p. 558) can also be used for this purpose.
   (*b*) Solvellæ Sodii Chloridi (B.P.C.). 1·296 g. in each. One dissolved in 150 ml. (5 fl. oz.) of sterilised water forms Normal Saline Solution.
   (*c*) Balneum Sodii Chloridi (B.P.C.). 1 in 40.
2. Sodii Carbonas (B.P.). 5–30 gr. (3–20 dg.).
   (*a*) Sodii Carbonas Exsiccatus (B.P.). 3–10 gr. (2–6 dg.).
3. Sodii Bicarbonas (B.P., U.S.P.). 5–30 gr. (3–20 dg.).
   (*a*) Trochiscus Sodii Bicarbonatis (U.S.P., B.P.C.). 3 gr. in each.
   (*b*) Sodii Citro-tartras Effeverscens (B.P.). 60–120 gr. (4–8 g.).
4. Sodii et Potassii Tartras, Soda Tartarata (B.P., U.S.P.). 120–240 gr. (8–16 g.).
   (*a*) Pulvis Sodæ Tartaratæ Effervescens (B.P.).
   (*b*) Pulvis Effervescens Compositus (U.S.P.).
5. Sodii Phosphas (B.P., U.S.P.). 30–240 gr. (2–16 g.).
   (*a*) Sodii Phosphas Effervescens (B.P., U.S.P.). 60–240 gr. (4–16 g.).
   (*b*) Sodii Phosphas Acidus (B.P.). 30–60 gr. (2–4 g.).
6. Sodii Sulphas (B.P., U.S.P.). 30–240 gr. (2–16 g.).
   (*a*) Sodii Sulphas Effervescens (B.P.). 60–240 gr. (4–16 g.).

Potassium.

1. Potassa Caustica (B.P.). Potassii Hydroxidum (U.S.P.).
   (*a*) Liquor Potassæ (B.P., U.S.P.). 5 per cent., 10–30 min. (6–18 dl.), freely diluted.
2. Potassii Chloridum (B.P.C.). 15–60 gr. (1–4 g.).
3. Potassii Carbonas (B.P., U.S.P.). 5–20 gr. (3–12 dg.).
4. Potassii Bicarbonas (B.P., U.S.P.). 5–30 gr. (3–20 dg.).
5. Potassii Citras (B.P., U.S.P.). 15–60 gr. (1–4 g.).
6. Potassii Acetas (B.P., U.S.P.). 15–60 gr. (1–4 g.).
7. Potassii Nitras (B.P., U.S.P.). 5–20 gr. (3–12 dg.).
8. Potassii Tartras (B.P.). 30–240 gr. (2–16 g.).
9. Potassii Tartras Acidus (B.P.). Potassii Bitartras (U.S.P.). 15–60 gr. (1–4 g.).
10. Potassii Sulphas (B.P., U.S.P.). 15–45 gr. 1–3 g.).
11. Potassii Chloras (B.P., U.S.P.). 5–15 gr. (3–10 dg.).
    (*a*) Trochischus Potassii Chloratis (B.P., U.S.P.). 3 gr. (2 dg.) in each.

Calcium.

1. Calx (B.P., U.S.P.).
2. Calcii Hydras (B.P., U.S.P.).
   (*a*) Liquor Calcis (B.P., U.S.P.). 1–4 fl. oz. (30–120 ml.).
   (*b*) Liquor Calcis Saccharatus (B.P.). 15–60 min. (1–4 ml.).
   (*c*) Syrupus Calcis (U.S.P.). 30 min. (2 ml.).
   (*d*) Linimentum Calcis (B.P., U.S.P.).
3. Calcii Chloridum (B.P.). 5–15 gr. (3–10 dg.).
4. Creta Præparata (B.P., U.S.P.). 15–60 gr. (1–4 g.).
   (*a*) Mistura Cretæ (B.P., U.S.P.). ½–1 fl. oz. (15–30 ml.).
   (*b*) Pulvis Cretæ Aromaticus (B.P.). 10-60 gr. (6–40 dg.).
   (*c*) Pulvis Cretæ Compositus (U.S.P.). 30 gr. (2 g.).
   (*d*) Pulvis Cretæ Aromaticus cum Opio (B.P.). 10–60 gr. (6–40 dg.).
5. Calcii Carbonas Præcipitatus (B.P., U.S.P.). 15–60 gr. (1–4 g.).
6. Calcii Phosphas (B.P., U.S.P.). 5–15 gr. (3–10 dg.).
7. Calcii Lactas (B.P.). 10–30 gr. (6–20 dg.).
   (*a*) Syrupus Calcii Lactophosphatis (B.P.). ½–1 fl. dr. (2–4 ml.).

(*b*) Liquor Calcii Lactatis (B.P.C.). 1–4 fl. dr. (4–15 ml.).

Calcium lactate possesses the double advantage of being freely soluble and non-irritant, and can therefore be injected hypodermically. Most of the other preparations are only slightly soluble, and calcium chloride, although freely soluble, is very irritant.

Lithium.

1. Lithii Carbonas (B.P., U.S.P.). 2–5 gr. (12–30 cg.).
   (*a*) Aqua Lithia (B.P.C.).
   (*b*) Granulæ Lithii Carbonatis (B.P.C.). 30–120 gr. (2–8 g.).
2. Lithii Citras (B.P., U.S.P.). 5–10 gr. (3–6 dg.).
   (*a*) Lithii Citras Effervescens (B.P., U.S.P.). 60–120 gr. (4–8 g.).
3. Lithii Chloridum (B.P.C.). 5–10 gr. (3–6 dg.).

None of these preparations is of any therapeutic value.

Ammonium.

1. Liquor Ammoniæ Fortis (B.P.). 32·5 per cent. Aqua Ammoniæ Fortior (U.S.P.). 28 per cent. NH_3.
   (*a*) Linimentum Camphoræ Ammoniatum (B.P.).
   (*b*) Spiritus Ammoniæ Aromaticus (B.P., U.S.P.). 20–40 min. (12–25 dl.), repeated; 60–90 min. (4–6 ml.), single.
   (*c*) Spiritus Ammoniæ Fetidus (B.P.). 20–40 min. (12–25 dl.), repeated; 60–90 min. (4–6 ml.), single.
   (*d*) Spiritus Ammoniæ (U.S.P.). 15 min. (1 ml.).
   (*e*) Tinctura Ammoniæ Composita (B.P.C.). 5–10 min. (3–6 dl.).
   (*f*) Liquor Ammoniæ Detergens (B.P.C.). Contains Oleic Acid and Alcohol.
2. Liquor Ammoniæ (B.P.). Aqua Ammoniæ (U.S.P.). 10 per cent.
   (*a*) Linimentum Ammoniæ (B.P., U.S.P.).
   (*b*) Liquor Ammoniæ Anisatus (B.P.C.). 15–60 min. (1–4 ml.).
3. Ammonii Chloridum (B.P., U.S.P.). 5–20 gr. (3–12 dg.).
   (*a*) Trochiscus Ammonii Chloridi (U.S.P.). 1 g. in each.
4. Ammonii Carbonas (B.P., U.S.P.). Expectorant, 3–10 gr. (2–6 dg.); Emetic, 30 gr. (2 g.).
5. Ammonii Bicarbonas (B.P.C.). 3–10 gr. (2–6 dg.).
6. Ammonii Acetas (B.P.C.). 10–30 gr. (6–20 dg.).
   (*a*) Liquor Ammonii Acetatis (B.P., U.S.P.). 2–6 fl. dr. (8–24 ml.).
7. Ammonii Citras (B.P.C.). 30–60 gr. (2–4 g.).
   (*a*) Liquor Ammonii Citratis (B.P.). 2–6 fl. dr. (8–24 ml.).
8. Ammonii Phosphas (B.P., 1898). 5–20 gr. (3–12 dg.).

Magnesium.

1. Magnesii Sulphas (B.P., U.S.P.). 30–240 gr. (2–16 g.).

For subdural injection, 3–10 c.c. of a 7·3 per cent. solution may be used. The other preparations of Magnesium are described under Saline Purgatives. A. J. C.

THE HEAVY METALS

With the doubtful exceptions of mercury and iron, the heavy metals are used medicinally only in the form of compounds, a usage which recognises the fact that the actual metals themselves are pharmacologically inert. It is only in the form of ions that the metals manifest pharmacological activity.

Of the heavy metals, copper, zinc, aluminium, lead, silver, iron and mercury will be discussed first, because they possess certain actions in common, chiefly local in effect. As these are the only actions which, in ordinary circumstances, certain of the group exhibit, the division of their pharmacology into local and general actions is convenient.

I.—Local Actions

These include all actions exerted on the skin and mucous membranes prior to absorption, *i. e.* while the substances are, strictly speaking, still outside the body.

When a *soluble* salt of a heavy metal is added to a solution of albumen, an albuminate is formed as a precipitate or coagulum: in this reaction the albumen takes the place of an acid in forming an insoluble salt of the metal, while the acid originally combined with the metal is set free.

The same kind of reaction takes place when a solution of a salt of a heavy metal comes in contact with a mucous membrane, the proteins of the cells forming an insoluble compound with the metal and the acid of the salt being liberated. As this reaction occurs actually in the substance of the cells, their vitality is modified to a greater or less extent; and, though the extent, or even the quality, of the change cannot always be foretold precisely, the effect produced depends chiefly upon three things: (1) the physical nature of the albuminate formed; (2) the inherent toxicity of the metal, and (3) the nature of the acid liberated.

The application of such a metallic solution may produce a coagulation merely of a superficial film of the proteins of the cells. This checks the normal secretion of these cells, partly mechanically but partly also by interfering with the chemical processes of secretion. To this superficial action whereby secretion is prevented the word *astringent* is applied, and the

term has a pharmacological justification in that the coagulated protein tends to condense and the tissue is thus "drawn together." This astringent action is one of the most important of the local effects of the heavy metals.

The reaction described may not, however, be limited to the surface of the cells, but may penetrate the cell substance more deeply and even penetrate through one or more layers of cells. In this case the metabolism of the affected cells is interfered with to such an extent that they die, and the metal then exerts a *caustic* action.

The amount of astringent action or the depth of the caustic action depends upon the nature of the albuminate formed. If the albuminate of a particular heavy metal is dense and compact, the superficial coagulum which first forms prevents further penetration, and the action tends to be purely astringent: if the reaction be of sufficient intensity the superficial cells may die, but the caustic action will be self-limited. On the other hand, if the albuminate be loose and flocculent, or especially if the albuminate be readily soluble in excess of albumen (which will almost certainly be present), then there is no such definite barrier to extensive action, and the astringent action will also be less powerful.

The intensity of the action is not, however, dependent solely upon the physical nature of the albuminate, because metals which differ from one another only slightly in regard to this point vary widely in the facility with which they destroy the life of cells. They vary in their "toxicity." This factor is obviously of special importance in determining the extent of caustic action.

These two factors determine the local actions of different metals. In local action, the metallic ion is not alone of importance, because its action is to a certain extent modified by the nature of the acid radicle, and the latter by itself may exercise an independent and by no means negligible action. This makes a difference in the behaviour of different compounds of the same metal. For in the first place the quickness and completeness of the interaction between a metallic ion and the cell protein will depend upon the degree to which the metal is ionised: the acid radicle, therefore, controls the specific action of the metal. In the second place, when the metallic ion combines with albumen and the acid ion is freed, though in ordinary circumstances the amount of this acid is small, it is liberated actually in the cell substance, and has, therefore, every opportunity of exerting its specific effect. Hence it is that salts of mineral acids exert a more powerful local action than salts of organic acids, both because the former are more completely ionised and because the specific action of the mineral acid is more powerful than that of the organic acid.

Solutions of metallic salts have all a more or less powerful *antiseptic* action. This is again due to their forming an albuminate with the proteins of the micro-organisms. The intensity of their antiseptic action is, therefore, dependent upon the three factors already mentioned, but of those the specific toxicity of the metal is probably of the greatest importance. A particular metal is not equally toxic to all micro-organisms. Further, if the order of toxicity of a series of metals be determined for one micro-organism, it will not hold good for another. Hence it is difficult, if not impossible, to arrange the heavy metals with accuracy in the order of their antiseptic power. However, generally speaking, mercury comes first with copper next, zinc and silver being also important antiseptics, while the antiseptic value of aluminium, iron and lead is distinctly less. Usually a particular heavy metal is not selected on account of its higher toxicity for a particular pathogenic organism, though pharmacological data are accumulating upon which such a therapeutic differentiation may be based.

Insoluble compounds of the heavy metals produce no immediate effect when added to solutions of albumen, but after prolonged contact with the tissues they slowly combine with the proteins and exert a milder astringent action. Similarly they have an antiseptic action which is also developed more slowly than with the soluble salts.

Therapeutically, salts of heavy metals are used locally in dilute solutions for their astringent and antiseptic actions to mucous membranes and wounds, etc., in concentrated solutions or in solid form as caustics. Insoluble compounds, especially oxides and carbonates, are used where a less powerful, but more prolonged, astringent or antiseptic action is desired, in the form of ointments or lotions.

Heavy metals, when swallowed, exert effects on the mucous membrane of the alimentary canal which vary from astringent to irritant and caustic. Thus lead acetate, even in considerable quantities, is simply astringent with very little irritation, so that it can be used as an intestinal astringent. The irritant, as distinct from caustic action, can be obtained with copper, zinc and aluminium, whence the use of their salts as emetics. In large quantities, and especially if concentrated, the heavy metals act as powerful irritants and corrosives of the alimentary canal.

II.—General Actions

When given by the mouth, the heavy metals are absorbed slowly and with difficulty, because they form insoluble albuminates. The small

amount absorbed circulates in the blood, probably as soluble combinations with protein. They are excreted chiefly by the mucous membrane of the alimentary canal, especially of the large intestine, and to a much less extent by the kidney. Smaller amounts of some metals may be eliminated by other glands, *e.g.* the salivary and mammary glands, mercury being exceptional in the wide range of its excretion. Excretion is usually even slower than absorption, and is also frequently extremely irregular both in time and in quantity. Hence such metals as are absorbed tend to accumulate in the tissues, being stored up in the liver, spleen, kidney, bone marrow and other organs.

The metals may conveniently be grouped according to the ease with which they are absorbed.

Thus copper, zinc and aluminium are absorbed in such small amounts that their general action is negligible. With single large doses, emesis is one factor which prevents absorption, but even prolonged ingestion of smaller doses of any of these three metals produces no effects of importance. They are used, therefore, almost exclusively for their local actions.

Similarly, lead and silver are used almost entirely for their action before absorption. Those metals, however, when administered over prolonged periods, are absorbed in sufficient quantity to give rise to very definite effects—a chronic poisoning, which in the case of lead is of great practical importance.

Iron and mercury are more readily absorbed; and while, like the other metals, they are employed medicinally for their local actions, unlike them they produce effects after absorption which are of the highest therapeutic value.

Copper, Zinc and Aluminium.—Of these three metals, the most widely used salt is the sulphate, in the case of aluminium a double sulphate, alum. They are used almost exclusively for their local actions, as astringents and antiseptics, especially for the mucous membranes of the eye, urethra, etc.

In the case of zinc, the soluble chloride is used as a caustic and cheap disinfectant; while the insoluble compounds of zinc, *e.g.* oxide and carbonate, are widely used in ointments and lotions for a milder and more prolonged astringent or antiseptic action.

Dried alum is occasionally used as a caustic, acting partly by abstracting water from the tissues.

Internally, small doses of those metals have been used as gastric astringents. In the doses given, most if not all of their astringent power is lost before they reach the intestine. Their chief use by the mouth is, however, as emetics, acting reflexly by irritation of the gastric mucous membrane. Copper sulphate is most frequently used as an emetic, but zinc sulphate is not inferior to it and is less irritating if emesis does not occur. Alum is a less reliable emetic.

Copper sulphate has a special use as an emetic in phosphorus poisoning, where it also renders any phosphorus retained in the stomach less soluble.

Zinc oxide has been used in chronic nervous diseases and to prevent sweating. There is no pharmacological evidence to warrant its being of the slightest value in either of those conditions, since it is absorbed to so slight an extent.

Preparations

Copper

Cupri Sulphas (B.P., U.S.P.). $\frac{1}{4}$–2 gr. (16–120 mg.) as an astringent; 5–10 gr. (3–6 dg.) as an emetic.
- Buginaria Cupri Sulphatis (B.P.C.). $\frac{1}{10}$ gr. Nasal Bougies.
- Guttæ Cupri Sulphatis. 0·5 per cent. Eye Drops.

Cupri Nitras (B.P.C.). $\frac{1}{12}-\frac{1}{6}$ gr.

Cupri Subacetas (B.P.C.).
- Unguentum Cupri Subacetatis (B.P.C.). 1 in 16.

Cupri Oleas.
- Unguentum Cupri Oleatis (B.P.C.). 1 in 8.

Zinc

Zinci Sulphas (B.P., U.S.P.). 1–3 gr. (6–20 cg.); as emetic, 10–30 gr. (6–20 dg.).
- Buginaria Zinci Sulphatis (B.P.C.). $\frac{1}{10}$ gr.
- Buginaria Zinci Sulphatis Composita (B.P.C.).
- Carbasus Zinci Sulphatis (B.P.C.). 5 per cent.
- Cereoli Zinci Sulphatis (B.P.C.). $1\frac{1}{2}$ gr.
- Collyrium Zinci Sulphatis (B.P.C.). 1 in 500.
- Injectio Sulphatum (B.P.C.).
- Injectio Zinci Sulphatis (B.P.C.). 6·8 in 100.
- Lamellæ Zinci Sulphatis (B.P.C.). $\frac{1}{250}$ gr.
- Lotio Rubra (B.P.C.). Red wash. 1 in 200.
- Lotio Zinci Sulphatis (B.P.C.). 1 in 200.
- Pulvis Zinci Sulphatis Compositus (B.P.C.).
- Solvellæ Zinci Sulphatis (B.P.C.). 4 gr.
- Solvellæ Zinci Sulphatis et Aluminis (B.P.C.). 10 gr. of each.
- Solvellæ Zinci Sulphatis Fortes. 20 gr. in each.

Zinci Acetas (B.P., U.S.P.). 1–2 gr. (6–12 cg.).

Zinci Bromidum (U.S.P., B.P.C.). 2–5 gr.

Zinci Carbonas (B.P.). Zinci Carbonas Præcipitatus (U.S.P.).

Zinci Chloridum (B.P., U.S.P.).
- Collodium Zinci Salicylicum (B.P.C.).
- Guttæ Zinci Chloridi et Cocainæ (B.P.C.).
- Injectio Zinci Chloridi (B.P.C.). 1 in 10.
- Liquor Zinci Chloridi (B.P., U.S.P.), 50 per cent. 75 per cent.
- Lotio Zinci Chloridi (B.P.C.). 1 in 400.

Zinci Iodidum (U.S.P.). Average dose, 1 gr. (65 mg.).
Zinci Oleas (B.P.C.).
Pulvis Zinci Oleatis Compositus (B.P.C.).
Unguentum Zinci Oleatis.
Zinci Oxidum (B.P., U.S.P.). 3–10 gr. (2–6 dg.
Cremor Zinci (B.P.C.). 3 in 20.
Emplastrum Zinci Oxidi (B.P.C.). 1 in 5.
Pasta Zinci Composita (B.P.C.). Lassar's Paste.
Pasta Zinci et Gelatini (B.P.C.). Unna's Paste.
Pasta Zinci et Ichthamolis (B.P.C.).
Pessus Zinci Oxidi (B.P.C.). 15 gr.
Pilula Zinci Oxidi et Belladonnæ (B.P.C.).
Pulvis Zinci et Acidi Borici (B.P.C.).
Pulvis Zinci et Acidi Salicylici (B.P.C.).
Pulvis Zinci et Amyli (B.P.C.).
Pulvis Zinci et Amyli Compositus (B.P.C.).
Unguentum Zinci (B.P., U.S.P.), 15 per cent., 20 per cent.
Zinci Peroxidum (B.P.C.).
Zinci Permanganas (B.P.C.).
Zinci Phosphidum (B.P.C.). $\frac{1}{20}-\frac{1}{4}$ gr.
Zinci Oleostearas (B.P.) and Zinci Stearas (U.S.P.).
Unguentum Zinci Stearatis (U.S.P.). 50 per cent.
Unguentum Oleostearas (B.P.).
Zinci Sulphocarbolas. Zinci Phenolsulphonas. 1–4 gr.
Lotio Zinci Sulphocarbolatis (B.P.C.). 7 in 1000.
Solvellæ Zinci Sulphocarbolatis (B.P.C.). 2 gr.
Solvellæ Zinci Sulphocarbolatis (B.P.C.). 10 gr.
Zinci Valerianas (B.P.). 1–3 gr. (6–20 cg.). Zinci Valeras (U.S.P.).
Pilulæ Zinci Valerianatis Compositæ (B.P.C.).
Tablettæ Zinci Valerianatis Compositæ (B.P.C.).

Alum

Alumen Purificatum (B.P.). 5–10 gr. (3–6 dg.).
Collyrium Aluminis (B.P.C.). 1 in 100.
Gargarisma Aluminis (B.P.C.). 1 in 48.
Glycerinum Aluminis (B.P.). 1 in 6.
Pessus Aluminis (B.P.C.). 15 gr.
Pessus Aluminis et Zinci (B.P.C.). 5 gr. of each.
Solvellæ Aluminis (B.P.C.). 10 gr.
Alumen Exsiccatum (B.P.).
Alumen Ferricum (B.P.C.). 5–10 gr.
Aluminii Acetas (B.P.C.).
Carbasus Aluminii Acetatis (B.P.C.). 3 per cent.
Liquor Aluminii Acetatis (B.P.C.). 6–11 min.
Aluminii Aceto-Tartras (B.P.C.).
Aluminii Chloridum (B.P.C.). 2–4 gr.
Aluminii Hydroxidum (U.S.P.).
Aluminii Naphthol-Sulphonas (B.P.C.). 4–8 gr.
Aluminii Subacetas (B.P.C.). 5–10 gr.
Aluminii Sulphas (U.S.P.). 2–5 gr.

Silver.—Albuminate of silver is particularly dense; partly on this account and also because they form an insoluble compound with the chlorides of the tissues, the astringent action of soluble silver salts, though powerful, is superficial. Concentrated solutions are caustic, but, for the same reasons, not penetrating. Silver salts are also powerful antiseptics.

Silver nitrate is by far the most important and the only official soluble salt. Externally, it is used, in dilute solution, as an astringent antiseptic. It is of supreme value as an application to the mucous membranes of the conjunctiva and urethra. It is used as a solid stick as a caustic, possessing the advantage that its action can be limited.

Internally, silver nitrate has been used as astringent in gastric ulcer. A great part of the small dose given must be converted in the stomach into insoluble chloride and thus presumably rendered inactive. If it possesses the virtues sometimes ascribed, it would seem to have some other action in gastric ulcer than mere astringency. Given by the mouth it has no astringent action on the intestine as it is rapidly reduced to metallic silver, but dilute solutions have been used as enemata in dysentery. When large quantities of silver nitrate are swallowed the usual symptoms of corrosion of the alimentary canal occur: burning pain in the throat and epigastrium, vomiting and usually diarrhœa with consequent collapse.

In such cases little if any of the silver is absorbed. When, however, smaller quantities of silver are continuously ingested for long periods, as was done formerly in the treatment of chronic nervous diseases, the metal may be absorbed in sufficient quantity to give rise to definite symptoms. In whatever way it gains entrance to the blood—and apparently it does so in a soluble form—the metal is finally stored up as an organic compound chiefly in the connective tissues. This compound has a dark colour and the tissues in which it is stored become pigmented. This pigmentation may occur in any organ, but for practical purposes the most important seat of deposit is the skin. A patient suffering from chronic silver poisoning presents a greyish, or more usually slate, colour of the skin. Once produced, this coloration cannot be eradicated, as the pigment is deposited in the deep layer of the skin, and cannot be attacked either by superficial solvents or by internal administration. The pigmentation can sometimes be seen in the mucous membrane of the mouth.

Anæmia and emaciation are also said to occur

in chronic silver poisoning, and the symptoms are called collectively "Argyria."

The occurrence even of pronounced pigmentation does not shorten life. Local pigmentation has been produced by continued application of solutions of silver nitrate to mucous membranes.

When it is desired to prescribe silver in chronic nervous diseases, the oxide is a convenient preparation; being insoluble, it does not cause irritation of the stomach, as does the nitrate.

One disadvantage attending the use of silver nitrate as an astringent or antiseptic is the amount of irritation it produces, due to its combining with the proteins of the tissues. To obviate this, in recent years protein combinations of silver have been introduced. In this way the local astringent and irritant action is very definitely reduced. On the other hand, there is also a reduction in antiseptic power which, however, may not be correspondingly great. Hence, while protein and similar combinations of silver have less local irritant action, they are also less efficient antiseptics, and it is not yet quite clear that they have any greater merit than silver nitrate itself used in greater dilution.

Silver

Argenti Nitras (B.P., U.S.P.). $\frac{1}{4}-\frac{1}{2}$ gr. (16–30 mg.).
- Argenti Nitras Fusus (U.S.P.).
- Argenti Nitras Induratus (B.P.).
- Argenti Nitras Mitigatus (B.P., U.S.P.). 1 in 3.
- Guttæ Argenti Nitratis (B.P.C.). $\frac{1}{2}$ per cent.
- Spiritus Argenti Nitratis (B.P.C.). 5 per cent. in spirit of nitrous ether.

Argenti Acetas (B.P.C.).
Argenti Citras (B.P.C.).
Argenti Cyanidum (B.P.C.). $\frac{1}{60}-\frac{1}{20}$ gr.
Argenti Oxidum (U.S.P.). 1 gr. (65 mg.).
Argenti Proteinatum (B.P.C.).

Lead.—The acetate is the only soluble salt of lead which is widely used medicinally. It differs from the soluble salts of the metals previously considered chiefly in being less irritant and having less antiseptic power. Indeed, acetate of lead is almost a pure astringent. The albuminate of lead is particularly dense and insoluble, and hence, as an astringent lead acetate is powerful but superficial. The two main reasons for the diminished irritant, antiseptic, and caustic actions of this salt, as compared with soluble salts of the other heavy metals, are that lead itself is comparatively non-toxic and also that it is combined with an organic acid, whereas, in the case of other heavy metals, salts of mineral acids are generally used.

Solutions of acetate of lead are applied for their astringent and sedative action to the skin and mucous membranes. Of the heavy metals, it is the most efficacious as an intestinal astringent. It is rarely used as a gastric astringent on account of its tendency to cause constipation, which it is usually desired to avoid in those cases where stomach astringents are necessary. In cases of diarrhœa and of intestinal hæmorrhages, however, it is widely used. In those conditions it is usually given in pill form and often combined with opium, as in the official pill. It acts as an astringent and hæmostatic both by coagulating the albumens of the discharges and of the secreting surface and also by contracting the smaller blood-vessels. It is well to note that poisonous effects have followed, *e.g.*, prolonged vaginal douching with solutions of lead acetate.

Preparations containing lead in the form of subacetate are also used for their local astringent action, but only externally. The subacetate of lead is even more astringent than the acetate. Acute poisoning by large quantities of lead acetate presents the characteristic symptoms of an irritant poison: nausea, vomiting, purging and collapse; but constipation is a not infrequent effect.

Chronic lead poisoning, which, owing to its frequency and the variety of symptoms to which it may give rise, is of great importance, may be induced in many ways, but is almost always due to the swallowing of lead in some form. Of the commoner causes of chronic lead poisoning may be mentioned the drinking of water, cider or beer, contaminated with lead, or the swallowing of lead in some form by lead workers, plumbers or compositors. The condition may arise, however, in a great variety of ways, some not readily detected.

In nearly all cases, however, small quantities of lead have been ingested for a considerable time, and, though absorption may be slow and incomplete, excretion is even less rapid, and the metal accumulates in the tissues and gives rise to toxic effects.

The symptoms which may be produced are so numerous that it is possible here to enumerate only the more important.

Among the early and fairly constant symptoms are a metallic taste in the mouth, loss of appetite, and often constipation. One symptom which is of diagnostic value is the appearance of a blue line at the margin of the gums, due to the formation there of sulphide of lead. The blue line may be rapidly produced and be present without any other symptom of lead poisoning. It always disappears slowly. Anæmia, characterised by basophilic changes in the red cells, which some regard as significant of lead poisoning, often occurs early and may be accompanied by cachexia.

Colic occurs frequently and usually early in

poisoning. It is characterised by the onset of severe, often sudden, pain (with intermissions) referred commonly to the umbilical region and usually relieved, but occasionally aggravated, by pressure. The colic appears to be due to the direct irritant action of lead on non-striped muscle, though the alleged beneficial effect of atropine suggests rather an action on some part of the nerve supply of the intestine.

The nervous system, both central and peripheral, is especially prone to be attacked by lead. The most common result of this is peripheral neuritis, which usually first affects the nerves supplying the extensors of the wrists and fingers but sparing the brachio-radialis. Sometimes the corresponding muscles of the foot and other muscles are affected. The paralysed muscles show the reaction of degeneration.

The sensory nerves may also be affected, giving rise to areas of hyperæsthesia or anæsthesia. Blindness, due to neuro-retinitis, occurs rarely but sometimes suddenly.

Brain symptoms of various kinds may occur, sometimes of sudden onset in workers in lead factories and simulating diverse types of cerebral disease, among which may be mentioned mania, melancholia and epileptiform convulsions—effects in part almost certainly due to a direct action of lead upon the brain cells.

Joints, especially the knee joint, are not infrequently affected with painful paroxysms. In most cases of prolonged lead poisoning arteriosclerosis with high blood pressure and interstitial nephritis are likely to occur. There is an undoubted but ill-defined association of gout with lead poisoning, and alcoholism also predisposes to it. In women suffering from lead poisoning abortion is frequent, and the use of lead as a criminal abortifacient is well known and increasing.

Lead

Plumbi Acetas (B.P.). 1–5 gr. (6–30 cg.).
- Lotio Plumbi (B.P.C.). 1 in 80.
- Lotio Plumbi Acetatis (B.P.C.). 1 in 200.
- Lotio Plumbi cum Opio (B.P.C.).
- Lotio Plumbi et Sulphuris (B.P.C.). Sulphur Hair Restorer.
- Lotio Plumbi Evaporans (B.P.C.).
- Pilula Plumbi cum Opio (B.P.). 2–4 gr. (12–25 cg.).
- Suppositoria Plumbi Composita (B.P.), contains 0·1 gr. of morphia.
- Tablettæ Plumbi cum Opio (B.P.C.).
- Ceratum Plumbi Subacetatis (B.P.C.).
- Glycerinum Plumbi Subacetatis (B.P.).
- Liquor Plumbi Subacetatis Fortis (B.P., U.S.P.). Goulard's Extract.
- Liquor Plumbi Subacetatis Dilutus (B.P., U.S.P.). Goulard's Lotion.
- Unguentum Plumbi Subacetatis (B.P.).

Plumbi Carbonas.
- Unguentum Plumbi Carbonatis. 10 per cent.

Plumbi Iodidum (B.P.).
- Pessus Plumbi Iodidi (B.P.C.). 5 gr.
- Unguentum Plumbi Iodidi (B.P.). 10 per cent.

Plumbi Nitras (U.S.P.).

Plumbi Oleas (B.P.C.).
- Ceratum Plumbi (B.P.C.). Pearson's Cerate.
- Emplastrum Plumbi (B.P., U.S.P.).
- Unguentum Diachylon (U.S.P.). Hebra's Ointment.
- Unguentum Diachylon Carbolisatum (B.P.C.). Lassar's Ointment.
- Unguentum Diachylon et Paraffini (B.P.C.). Kaposi's Diachylon Ointment.
- Unguentum Diachylon Salicylatum (B.P.C.). Hebra's Salicylated Ointment.

Plumbi Oxidum (B.P., U.S.P.).

Mercury.—In addition to mercuric and mercurous compounds, preparations containing metallic mercury are widely used therapeutically.

Soluble mercuric salts, like the perchloride, approximate in local action to the soluble salts of the other heavy metals, with certain differences. Thus, they coagulate albumen, but the albuminate formed differs from the other albuminates in being much more soluble in excess of albumen. Hence, solutions of mercury salts are almost non-astringent because, compared with the amount of mercury used, an excess of albumen will always be present. For the same reason stronger solutions act as very penetrating caustics, no permanent barrier of insoluble albuminate being formed, so that the amount of action is difficult to control. Hence salts of mercury are not used as astringents or caustics.

Mercury is used locally chiefly for its antiseptic action, in which it excels all the other heavy metals. The high antiseptic power of mercury is due partly to its enhanced power of penetrating cells, but chiefly to its specific toxicity. Solutions of the perchloride and other soluble salts are widely used as disinfectants and surgical antiseptics.

Insoluble salts of mercury, while much less energetic, are also antiseptic, and are especially indicated when a more prolonged antiseptic action is desired, *e. g.* in the treatment of many skin diseases. Mercury also acts as a powerful poison to more highly organised parasites, *e. g.* pediculi.

Taken internally, mercury has a specific irritant action on the intestine, probably not shared by the other heavy metals, whereby purgation is produced. This effect is exhibited

in a drastic form by the perchloride, and in a more mitigated form by calomel and certain metallic preparations. The effect is partly due to immediate local irritation, but partly also to remoter stimulation of the intestinal glands by the mercury which is absorbed. Calomel is widely used for this action. As a rule it does not produce colic and is reputed to affect the small intestine more than the large intestine. Preparations made from metallic mercury (grey powder and blue pill) are also used as purgatives, their action being milder than that of calomel. Grey powder is a valuable purgative for young children.

It was at one time believed that calomel is changed into perchloride in the stomach and only then becomes active, and that grey powder, which contains some mercurous oxide, is changed first into calomel and then into perchloride. Though these changes would conveniently explain the gradations in their activity, it is doubtful if they take place. There is no clear evidence that calomel is changed in the stomach into perchloride, and this is not necessary to explain its activity, because even insoluble preparations of mercury seem to combine directly with albumen, though more slowly than the soluble preparations.

Mercury is also an effective intestinal antiseptic. In some intestinal conditions calomel is superior to any other antiseptic, *e. g.* in so-called "biliousness," which is now regarded as due to intestinal putrefaction.

Mercury has long been regarded as a cholagogue, and, though there is no evidence of a direct action on the liver increasing the formation of bile, it may lessen the reabsorption of bile by hurrying the passage of the contents through the small intestine.

Mercury, especially in its soluble compounds, is absorbed much more readily than other heavy metals. This is due partly to the solubility of its albuminate in excess of albumen and in solutions of sodium chloride and partly to the volatility of the metal and its salts. Probably a soluble salt like the perchloride is absorbed as a soluble albuminate: an insoluble salt like calomel may be first changed into a soluble albuminate and absorbed as such, or absorbed more directly by leucocyte ingestion.

Mercury is also absorbed readily from the skin. With this object fatty preparations, *e. g.* blue ointment, are rubbed into the skin, when the metal either uncombined or in the form of oleate penetrates the hair follicles and sebaceous glands and is absorbed by them.

For its action after absorption mercury is used chiefly in the treatment of syphilis. It acts as a specific poison to the spirochæta pallida.

In medicinal doses it has no important action on organs other than those by which it is excreted. It has a wide range of excretion, traces having been found in all the secretions which have been examined. It is eliminated chiefly, however, by the intestinal glands, salivary glands and kidney. Excretion is irregular in time and quantity and may continue with intermissions for long periods after cessation of administration. It may also disappear from one excretion and reappear in another.

It tends to excite the activity of all the glands by which it is eliminated. Of therapeutic importance is its action on the kidney. In certain conditions mercury is a powerful diuretic, calomel being the salt most frequently used. Various explanations have been given of the diuresis. According to some it is the result of a slight irritation of the secreting epithelium of the kidney, a reasonable hypothesis, since larger doses may cause very marked irritation of this organ. Another view is that the diuresis is secondary to the hydræmia produced by reabsorption of water from the glands of the alimentary tract, and therefore it is more pronounced if longer time be given for its absorption, *e. g.* by simultaneous administration of opium. In whatever way the effect is produced, there can be no doubt that in cases of cardiac dropsy calomel is a valuable, and sometimes very effective, diuretic.

Poisoning may be produced either by taking a single large dose of mercury or by taking repeated small doses.

In acute poisoning by ingestion of a soluble salt of mercury like the perchloride, the symptoms come on within a few minutes. The act of swallowing produces a sense of constriction or suffocation and burning pain in the throat and gullet. This is followed almost invariably by pain in the abdomen, with frequent vomiting and purging, the evacuations being usually streaked with blood. Symptoms of collapse follow of the usual type consequent upon corrosive irritation of the alimentary canal. Death may occur in a few hours, but usually in from one to five days, and occasionally even later. When death is delayed the symptoms merge into those of chronic poisoning, due to absorption of mercury.

Chronic poisoning from continued absorption of small quantities is of greater importance, because it may arise accidentally during medicinal administration. It may occur from any method of giving mercury.

The earliest and most prominent symptoms are exhibited by the secreting organs. One of the most important is salivation. This is probably partly due to a stimulation of the salivary glands by the absorbed mercury. The amount of saliva secreted may be enormous

and lead to fatal results from exhaustion. There may also occur loosening of the teeth, ulceration of the gums, and even gangrene of the lips and cheek and necrosis of the jaw. Formerly a mild degree of those symptoms, such as slight salivation and tenderness of the gums, was anticipated in the routine treatment of syphilis by mercury, now they are as far as possible avoided. Profuse salivation is more likely to arise when there is coincident disease of the kidney.

There are usually present also symptoms of irritation of the stomach and intestine, loss of appetite, nausea and diarrhœa, more rarely vomiting and constipation.

The urine may be at first increased, but later nephritis is often set up with albuminuria. Especially in the late stages of acute poisoning there may be marked diminution, or even complete suppression, of urine. Actual necrosis of the kidney epithelium may be induced, with deposit of calcium phosphate and carbonate in the necrosed cells.

Skin rashes not infrequently occur with mercury, more commonly when it is applied externally, but also from any other method of administration. The type of the eruption varies, and its appearance is often accompanied by some rise of temperature. Some people are much more liable to mercurial rashes than others.

Rarely, by long-continued medicinal administration, but more often in workers in mercury, a kind of chronic poisoning may arise which is usually ushered in by symptoms of subacute poisoning, *e. g.* salivation or diarrhœa, but which eventually affects chiefly the central nervous system. The chief symptoms are tremor of certain muscles, usually affecting the muscles of the hand and face first, and consisting of fine movements aggravated by voluntary effort. Later the movements may be continuous and epileptiform in nature. The electrical excitability of the muscles is unchanged, the cutaneous and tendinous reflexes are increased. Various sensory disturbances have also been described. A peculiar psychical condition (erythysmus mercurialis) sometimes occurs, characterised by a peculiar mental irritability. Nervous symptoms are most liable to occur when mercury is inhaled in toxic quantities, when they may be rapidly induced.

Children bear mercury well. It is stated that patients suffering from gout, phthisis or kidney disease are unusually intolerant of mercury.

Owing to the variety of ways in which it is administered, special mention must be made of the use of mercury in syphilis. The object to be aimed at, as in the treatment of all diseases of this type, is to obtain a maximum toxic effect upon the parasite with the minimum deleterious effect upon the tissues of the host. The toxic effect depends upon the concentration of the solution to which the parasite is exposed and the time for which it acts. The ideal aimed at is to get the highest concentration of mercury in the blood short of damaging the host, and to keep the concentration at or near this point for sufficiently long to kill the parasites. Which method of administering mercury comes nearest to this ideal is not yet decisively settled.

One of the commonest methods is still that of giving it by the mouth, the metallic preparations, blue pill and grey powder, being usually selected, though calomel and even corrosive sublimate have been used. The disadvantages of this method are that it produces the maximum disturbance of the alimentary canal, and that the mercury is absorbed somewhat slowly, and the amount is variable and uncertain.

Another method is by inunction, blue ointment, which is often selected, being rubbed into the skin of different areas of the body in rotation. Mercurial soaps, plasters or lints may also be applied to the skin to this end. The disadvantages of this method are that it is somewhat uncleanly, that it may give rise to disturbances of the skin, and also that absorption is somewhat slow, and no doubt variable. On the other hand it avoids, as far as possible, disturbance of digestion, and it ensures a very continuous presence of mercury in the blood and tissues.

A more recent method of introducing mercury into the system is by subcutaneous or intramuscular injection. When soluble preparations of mercury are used this method has the advantage of rapidity of action and certainty of dose. On the other hand the local reaction set up is often severe, and the method is painful. When insoluble salts are used the immediate pain is less but it may become severe when the insoluble preparation becomes changed into a soluble form. There is also the danger of abscess formation. The chief merit of the insoluble preparation is that as absorption is slow the injection need only be given say once a week. Injections also avoid to a large extent disturbance of the digestive organs.

Mercury is less frequently given by inhalation, *e. g.* of volatilised calomel. Some of the mercury is also deposited on the skin and then absorbed. This method affords the least certainty in regard to dosage and is, therefore, deservedly little used. Even when mercury is applied by inunction, some of the mercury is absorbed by inhalation in a volatile form.

Mercury

Hydrargyri Cyanidum (B.P.C.). $\frac{1}{16}-\frac{1}{8}$ gr.
Hydrargyri et Potassii Iodidum (B.P.C.). $\frac{1}{32}-\frac{1}{16}$ gr.
Solvellæ Hydrargyri et Potassii Iodidi. $2\frac{1}{2}$ gr.
Solvellæ Hydrargyri et Potassii Iodidi Fortes (B.P.C.). $8\frac{3}{4}$ gr.
Hydrargyri et Zinci Cyanidum (B.P.C.). Lister's Salt.
Carbasus Hydrargyri et Zinci Cyanidi (B.P.C.). Double Cyanide Gauze.
Gossypium Hydrargyri et Zinci Cyanidi. Cyanide Wool.
Hydrargyri Iodidum Flavum (U.S.P.). $\frac{1}{5}$ gr. (10 mg.).
Unguentum Hydrargyri Iodidi Flavi (B.P.C.). 1 in 8.
Hydrargyri Iodidum Rubrum (B.P., U.S.P.). $\frac{1}{32}-\frac{1}{16}$ gr. (2–4 mg.).
Gossypium Hydrargyri Iodidi (B.P.C.). 1 in 1000.
Unguentum Hydrargyri Iodidi Rubri (B.P.). 4 per cent.
Hydrargyri Iodidum Viride (B.P.C.). $\frac{1}{6}$–1 gr.
Hydrargyrum Oleatum (B.P.). Oleatum Hydrargyri (U.S.P.).
Oleinatum Hydrargyri. 20 per cent.
Unguentum Hydrargyri Oleati (B.P.). 1 in 4.
Hydrargyri Nitras.
Liquor Hydrargyri Nitratis Acidus (B.P.). 33·3 per cent.
Unguentum Hydrargyri Nitratis (B.P.). Citrine Ointment. 6·6 per cent. (U.S.P.) 7 per cent.
Unguentum Hydrargyri Nitratis Dilutum (B.P.). 1·3 per cent.
Unguentum Hydrargyri Nitratis Mitius (B.P.C.).
Hydrargyri Oxidum Flavum (B.P., U.S.P.).
Lotio Hydrargyri Flava (B.P.). Yellow Wash.
Oculentum Flavum (B.P.C.). 10 per cent.
Oculentum Flavum cum Atropina (B.P.C.).
Unguentum Hydrargyri Oxidi Flavi (B.P., U.S.P.). 10 per cent.
Unguentum Hydrargyri Oxidi Flavi Humidi (B.P.C.). 10 per cent.
Hydrargyri Oxidum Nigrum (B.P.C.).
Lotio Hydrargyri Nigra (B.P.). Black Wash.
Hydrargyri Oxidum Rubrum B.P., U.S.P.).
Unguentum Hydrargyri Oxidi Rubri (B.P., U.S.P.). 10 per cent.
Hydrargyri Oxycyanidum (B.P.C.). $\frac{1}{16}-\frac{1}{6}$ gr.
Hydrargyri Perchloridum (B.P.). $\frac{1}{32}-\frac{1}{16}$ gr. Corrosive Sublimate. Hydrargyri Chloridium Corrosivium (U.S.P.).
Carbasus Hydrargyri Perchloridi (B.P.C.). 1 in 1000.
Collyrium Hydrargyri Perchloridi (B.P.C.). 1 in 5000.
Glycerinum Hydrargyri Perchloridi (B.P.C.). 2 in 5.
Glycerinum Hydrargyri Perchloridi Alcoholicum (B.P.C.). 7 in 20.
Gossypium Hydrargyri Perchloridi (B.P.C.). 0·5 per cent. Sublimate Wool.
Injectio Hydrargyri Perchloridi Hypodermica (B.P.C.). 2–8 min.
Liquor Hydrargyri et Ammonii Chloridi (B.P.C.). 10 per cent. Hart's Solution.
Liquor Hydrargyri Perchloridi (B.P.). $\frac{1}{2}$–1 dr. (2–4 mils.).
Lotio Hydrargyri Acetica (B.P.C.). 1 in 1000.
Lotio Hydrargyri Perchloridi (B.P.C.). 1 in 500.
Lotio Hydrargyri Perchloridi Concentrata (B.P.C.). 1 in 100.
Solvellæ Hydrargyri Perchloridi (B.P.C.). $8\frac{3}{4}$ gr.
Solvellæ Hydrargyri Perchloridi Fortes (B.P.C.). $17\frac{1}{2}$ gr.
Solvellæ Hydrargyri Perchloridi Mites (B.P.C.). $2\frac{1}{3}$ gr.
Solvellæ Hydrargyri Perchloridi Parvæ (B.P.C.). $\frac{1}{2}$ gr.
Hydrargyri Persulphas (B.P.C.).
Hydrargyri Salicylas (B.P.C.). $\frac{1}{24}-\frac{1}{3}$ gr.
Hydrargyri Subchloridum (B.P.). Hydrargyri Chloridum Mite (U.S.P.). $\frac{1}{2}$–5 gr. (3–30 cg.).
Injectio Calomelanos (B.P.C.). 5–20 min. intra-muscularly.
Pilula Hydrargyri Subchloridi Composita (B.P.). 4–8 gr. (25–50 cg.). Plummer's Pill.
Pilulæ Calomelanos et Colocynthidis (B.P.C.).
Pilulæ Calomelanos Colocynthidis et Hyoscyami (B.P.C.).
Pulvis Calomelanos et Acidi Borici (B.P.C.). 1 in 4.
Pulvis Calomelanos et Amyli (B.P.C.). 1 in 4.
Pulvis Calomelanos et Zinci Oxidi (B.P.C.). 1 in 4.
Pulvis Hydrargyri Subchloridi Compositus 4–8 gr. (B.P.C.).
Tablettæ Hydrargyri Subchloridi (B.P.C.).
Tablettæ Hydrargyri Subchloridi Compositæ (B.P.C.).
Unguentum Hydrargyri et Plumbi et Zinci (B.P.C.). Unguentum Metallorum.
Unguentum Hydrargyri Subchloridi (B.P.). 1 in 5.
Unguentum Hydrargyri Subchloridi Forte (B.P.C.). 1 in 4.
Hydrargyri Succinimidum.
Injectio Hydrargyri Succinimidi Hypodermica (B.S.C.). 6–12 min.
Hydrargyri Sulphidum Nigrum (B.P.C.). 5–20 gr.
Hydrargyri Sulphidum Rubrum (B.P.C.).
Hydrargyri Tannas (B.P.C.). 1–2 gr.

Hydrargyrum (B.P., U.S.P.).
- Emplastrum Hydrargyri (B.P.). 1 in 3; (U.S.P.) 3 in 10.
- Injectio Mercurialis (B.P.C.). 5–20 min.
- Linimentum Hydrargyri (B.P.). 1 in 10.
- Massa Hydrargyri (U.S.P.). 4 gr. (250 mg.). 1 in 3.
- Oleum Cinereum (B.P.C.). 1–2 min. 2 in 5.
- Parogenum Hydrargyri (B.P.C.). 3 in 10.
- Pessus Hydrargyri (B.P.C.).
- Pilula Hydrargyri (B.P.). 4–8 gr. (25–50 cg.). 1 in 3. Blue Pill.
- Pilulæ Hydrargyri cum Opio (B.P.C.).
- Pilulæ Hydrargyri cum Rheo (B.P.C.).
- Unguentum Hydrargyri (B.P.). 3 in 10; (U.S.P.) 1 in 2.
- Unguentum Hydrargyri Compositum (B.P.). 12 per cent.
- Unguentum Hydrargyri Dilutum. 1 in 3 (U.S.P.).
- Unguentum Mercuriale (B.P.C.). 1 in 6.
- Unguentum Mercuriale Fortius (B.P.C.). 1 in 2.

Hydrargyrum Ammoniatum (B.P., U.S.P.).
- Cremor Hydrargyri Ammoniati Compositus B.P.C.).
- Oculentum Hydrargyri Ammoniati (B.P.C.). 1 in 100.
- Unguentum Hydrargyri Ammoniati (B.P.). 1 in 20; (U.S.P.) 1 in 10.
- Unguentum Hydrargyri Ammoniati Dilutum. 1 in 40.

Hydrargyrum cum Creta (B.P., U.S.P.). 1–5 gr. (6–30 cg.). 1 in 3, Grey Powder.
- Pilulæ Hydrargyri cum Creta et Opii (B.P.C.).
- Tablettæ Hydrargyri cum Creta (B.P.C.).

Iron.—Iron differs from the other heavy metals in being an important and essential normal constituent of the body, and it is upon this fact that its chief use in therapeutics depends.

Both ferrous and ferric salts are used medicinally, and in regard to their local actions they resemble salts of the other heavy metals. This is especially true in regard to ferric salts, which powerfully coagulate albumen and in suitable concentrations are useful and effective astringents. Ferrous salts have little or no tendency to coagulate albumen, as they form soluble compounds with it. Salts of iron in either form are also antiseptic, but they have a very limited usefulness in this direction. Ferric salts are employed chiefly as local hæmostatics, arresting hæmorrhage by coagulating blood albumens and so favouring the formation of clot. Internal administration of iron is, of course, useless for distant hæmorrhage, it must be applied directly to the bleeding surface.

When swallowed, iron salts exert an astringent action on the mucous membrane of the stomach and intestine, being more astringent and irritating when the iron is in the ferric condition, and when the salt is soluble. In some people medicinal doses of iron, especially of its more irritant compounds, produce indigestion, probably due to local irritation rather than to interference with the activity of the digestive ferments. Ordinary doses also tend to cause constipation by diminishing the intestinal secretions; the fæces are usually blackened from the formation of sulphide and tannate of iron.

Large amounts, especially if undiluted, cause severe gastro-enteritis with vomiting and diarrhœa.

The total amount of iron in the body of an adult man is estimated to be about 2·5 grammes. Most of it is contained in the hæmoglobin of the red blood cells, but a certain amount of extravascular iron is present in the liver and bone marrow especially, with traces probably in all organs. A very small proportion, *e. g.* a few milligrammes a day, is being constantly excreted, and the loss is replaced by the iron in the food, which usually contains sufficient for that purpose. The iron in the food is presented in the form of organic compounds which can be readily absorbed. In pathological conditions characterised by a fall in the amount of hæmoglobin (and, therefore, of the amount of iron) in each red blood corpuscle, clinical experience has proved that the administration of inorganic iron can restore the hæmoglobin to its normal amount. This suggests that inorganic iron, too, is absorbed and can be converted into a form which is available for the manufacture of hæmoglobin. Owing, however, to difficulties in explaining the absorption of inorganic iron, and as its administration does not increase the iron excreted in the urine, attempts have been made to explain the beneficial effects of inorganic iron in anæmia in other ways; but there is now no doubt that inorganic iron is absorbed and the steps in the process are now to some extent understood.

When taken into the stomach, iron salts are probably partly converted into chlorides. Ferric salts also tend to be reduced in the alimentary canal into ferrous. In the upper part of the intestine some of the iron will be converted into carbonate and in the large intestine most of it will be changed into sulphide. Most of the inorganic iron passes through unabsorbed and is excreted with the fæces as sulphide.

It has been shown that iron is absorbed by a limited part of the small intestine—the duodenum and the upper part of the jejunum—but little is known in regard to the actual condition in which it is absorbed, though it is probably as a soluble ferrous albuminate. It is then taken up by the leucocytes from the epithelial cells of the villi and carried into the

blood, to be deposited in various organs. Apparently it is first taken up by the spleen and later by the liver, and, in all probability, it is in the latter organ that the complex synthesis into hæmoglobin takes place. Whether or not the final stages of this synthesis are affected in the liver is not definitely known, but there can be little doubt that the precursors of hæmoglobin are formed here and transferred to the blood-forming organs when required. If the excess of iron be not required it is again given up by the liver to the blood to be excreted.

Under ordinary conditions iron is excreted chiefly by the epithelium of the large intestine and cæcum, though small amounts also appear in the urine, bile and possibly other secretions. When abnormal amounts of iron are absorbed the excess is eliminated by the intestinal epithelium; the amount of iron in the urine does not increase. The iron is excreted in organic combinations.

In medicinal doses, iron produces no pharmacological effects after absorption apart from the indirect results of restoring the blood to a more healthy condition.

Though the sphere of its use is limited, iron occupies a position of the highest importance in therapeutics because it stands alone as a remedy. Its use is practically confined to the treatment of simple anæmias, primary or secondary, in which the essential abnormality is a diminution of hæmoglobin in the red cells. In the treatment of chlorosis, the most important of this group of anæmias, the administration of iron is followed by beneficial results so certain and striking as to entitle it to a position among the most successful of remedial agents. The chief reason for its success is that iron acts in those diseases partly at all events as a necessary food. There is no unequivocal evidence that it acts in any other way, *e. g.* as a stimulant in the pharmacological sense to the blood-forming organs. Iron is also used as a "tonic" in convalescence from debilitating diseases, but its action here is the result of its improving the condition of the blood.

Iron in any form and administered in any way that admits of its absorption can be used successfully in the treatment of simple anæmias. Thus chlorosis can be cured even by giving the insoluble sulphide by the mouth as well as by subcutaneous, intravenous or intraperitoneal injection of suitable compounds. No method, however, is superior to the established one of oral administration.

The iron salts are not equally effective in treatment. In treating a disease like chlorosis, which is usually accompanied by impaired digestion and a distinct tendency to constipation, the indications are for the employment of non-irritant and non-astringent preparations of iron, and clinical experience has confirmed this in deciding upon the use, *e. g.*, of ferrous, in preference to ferric, salts. Thus ferrous carbonate (Blaud's pill) and reduced iron are among the most favoured preparations.

Various organic preparations of iron have also been used in the treatment of anæmia, such as hæmoglobin itself. Most authorities are agreed that hæmoglobin and its congeners are less useful in the treatment of anæmia than are the inorganic preparations. It is highly improbable that hæmoglobin or similar substances can be absorbed as such, and therefore it is improbable that by giving them the body is spared either destructive or synthetic processes.

Iron

Ferri Albuminas (B.P.C.). 3–10 gr.
  Liquor Ferri Albuminatis (B.P.C.). 1–4 dr.
Ferri Cacodylas (B.P.C.). $\frac{1}{4}$–1 gr.
Ferri Carbonas Saccharatus (B.P., U.S.P.). 10–30 gr. (6–20 dg.).
  Granulæ Ferri Carbonatis (B.P.C.). 30–60 gr.
  Massa Ferri Carbonatis (U.S.P.). 4 gr. (250 mg.).
  Mistura Ferri Carbonatis Composita (B.P.C.). $\frac{1}{2}$–1 fl. oz.
  Mistura Ferri Composita (B.P., U.S.P.). $\frac{1}{2}$–1 fl. oz. (15–30 mils.).
  Pilula Ferri (B.P.), Pilula Ferri Carbonatis (U.S.P.). 5–15 gr. (3–10 dg.).
  Tablettæ Ferri (B.P.C.).
  Tablettæ Ferri Carbonatis (B.P.C.).
Ferri Citras. U.S.P. average dose 4 gr. (250 mg.).
Ferri Citro-Arsenis Ammoniatus (B.P.C.). $\frac{1}{40}$–$\frac{1}{2}$ gr.
Ferri et Ammonii Citras (B.P., U.S.P.). 5–10 gr. (3–6 dg.).
  Granulæ Ferri et Ammonii Citratis (B.P.C.). 90–180 gr.
  Mistura Ferri Arsenicalis (B.P.C.). $\frac{1}{2}$–1 fl. oz.
  Vinum Ferri Citratis (B.P.), Vinum Ferri (B.P.). 1–4 dr. (4–16 mils.).
Ferri et Ammonii Citras Viridis (B.P.C.). 5–10 gr.
Ferri et Ammonii Tartras (U.S.P.). 4 gr. (250 mg.).
Ferri et Quininæ Citras (B.P., U.S.P.). 5–10 gr. (3–6 dg.).
  Granulæ Ferri et Quininæ Citratis (B.P.C.). 60–120 gr.
  Vinum Ferri Amarum (U.S.P.). 2 fl. dr. (8 c.c.).
  Vinum Ferri et Quininæ (B.P.C.). 1–4 fl. dr.
Ferri et Quininæ Citras Solubilis (U.S.P.). 4 gr. (250 mg.).
Ferri et Strychninæ Citras (U.S.P.). 2 gr. (125 mg.).
Ferri Formas (B.P.C.). 1–5 gr.

Ferri Glycerophosphas (B.P.C.). 1–5 gr.
Ferri Hydroxidum (U.S.P.).
Ferri Hydroxidum cum Magnesii Oxido (U.S.P.). Dose as arsenical antidote, 4 fl. oz. (120 c.c.).
Ferri Hypophosphis (B.P.C.). 1–3 gr.
Liquor Ferri Hypophosphitis Fortis (B.P.C.). 10–30 min.
Syrupus Ferri Hypophosphitis (B.P.C.). ½–2 fl. dr.
Ferri Iodidum (B.P.C.). 1–5 gr.
Liquor Ferri Iodidi Fortis (B.P.C.). 2–8 min.
Pilulæ Ferri Iodidi. 2 pills.
Syrupus Ferri Iodidi (B.P.), 7 per cent. ½–1 fl. dr. (2–4 mils.). (U.S.P.) 5 per cent., average dose 15 min. (1 c.c.).
Ferri Lactas (B.P.C.). 2–10 gr.
Ferri Oxidum Magneticum (B.P.C.). 5–10 gr.
Ferri Oxidum Saccharatum (B.P.C.). 10–30 gr.
Ferri Peptonas (B.P.C.). 5–10 gr.
Liquor Ferri Peptonatis (B.P.C.). 1–4 fl. dr.
Liquor Ferri Peptonatis cum Mangano (B.P.C.). 1–4 fl. dr.
Ferri Perchloridum (B.P.C.), Ferri Chloridum (U.S.P.). 1 gr. (65 mg.).
Glycerinum Ferri Perchloridi (B.P.C.).
Gossypium Ferri Perchloridi (B.P.C.).
Linteum Stypticum (B.P.C.).
Liquor Ferri Chloridi (U.S.P.). 1½ min. (0·1 c.c.).
Liquor Ferri Oxychloridi (B.P.C.). 10–30 m.
Liquor Ferri Perchloridi (B.P.). 5–15 min. (3–10 d.mil.).
Liquor Ferri Perchloridi Fortis (B.P.).
Mistura Ferri Amara (B.P.C.). ½–1 fl. oz.
Mistura Ferri Ammoniata (B.P.C.). ½–1 fl. oz.
Mistura Ferri et Magnesii Sulphatis (B.P.C.). ½–1 fl. oz.
Mistura Ferri Perchloridi (B.P.C.). ½–1 fl. oz.
Nebula Ferri Perchloridi (B.P.C.). 1 in 100.
Pigmentum Ferri Perchloridi (B.P.C.). 1 in 8.
Syrupus Ferri Subchloridi (B.P.C.). ½–1 fl. dr.
Tinctura Ferri Chloridi (U.S.P.). 8 min. (0·5 c.c.).
Tinctura Ferri Perchloridi (B.P.). 5–15 min. (3–10 d.mil.).
Ferri Phosphas Saccharatus (B.P.). 5–10 gr.
Liquor Ferri Phosphatis (B.P.C.).
Pilulæ Ferri Phosphatis cum Quinina et Strychnina (B.P.C.). 1 pill.
Syrupus Ferri Phosphatis (B.P.). ½–1 fl. dr. (2–4 mils.).
Syrupus Ferri Phosphatis Compositus (B.P.C.). ½–2 fl. dr. Chemical Food: Parrish's Syrup.
Syrupus Ferri Phosphatis cum Quinina et Strychnina (B.P.). ½–1 fl. dr. (2–4 mils.). Easton's Syrup.
Syrupus Triplex (B.P.C.). ½–1 fl. dr.
Tablettæ Ferri Phosphatis cum Quinina et Strychnina (B.P.C.).
Ferri Phosphas Solubilis (U.S.P.). 4 gr. (250 mg.).
Elixir Ferri Quininæ et Strychninæ Phosphatum (U.S.P.). 1 fl. dr. (4 c.c.).
Glyceritum Ferri Quininæ et Strychninæ Phosphatum. 15 min.
Syrupus Ferri Quininæ et Strychninæ Phosphatum. 1 fl. dr. (4 c.c.).
Ferri Pyrophosphas Solubilis (U.S.P.). 4 gr. (250 mg.).
Ferri Quininæ et Strychninæ Citras (B.P.C.). 2–5 gr.
Ferri Sulphas (B.P., U.S.P.). 1–5 gr. (6–30 cqm.).
Liquor Ferri Persulphatis (B.P.).
Liquor Ferri Subsulphatis (U.S.P.). 3 min. (0·2 c.c.).
Liquor Ferri Tersulphatis (U.S.P.). 3 min. (0·2 c.c.).
Mistura Ferri Aperiens (B.P.C.). ½–1 fl. oz.
Ferri Sulphas Exsiccatus (B.P., U.S.P.). ½–3 gr. (3–10 cqm.).
Pilulæ Ferri et Arsenici (B.P.C.). 1 or 2 pills.
Pilulæ Ferri et Quininæ et Nucis Vomicæ (B.P.C.). 1 or 2 pills.
Ferri Sulphas Granulatus (U.S.P.). 3 gr. (200 mg.).
Ferri Valerianas (B.P.C). 1–5 gr.
Pilulæ Ferri Valerianatis Compositæ (B.P.C.). 1 or 2 pills.
Ferrum (B.P.).
Syrupus Ferri Bromidi (B.P.C.). ½–1 fl. dr.
Syrupus Ferri Bromidi cum Quinina et Strychnina (B.P.C.). ½–1 fl. dr.
Vinum Ferri (B.P., U.S.P.). 1–4 fl. dr. (4–16 mils.).
Ferrum Redactum (B.P.), Ferrum Reductum (U.S.P.). 1–5 gr. (6–30 cgm.).
Trochiscus Ferri Redacti (B.P.). 1 gr. (0·06 gm.).
Ferri et Potassii Tartras (B.P., U.S.P.). 5–10 gr. (3–6 dg.).

Manganese.—Manganese has no known pharmacological actions which can render it of therapeutic value, and it is, therefore, of little medicinal importance.

It has been recommended in chlorosis and in certain uterine conditions, but it is very doubtful if it possesses the actions ascribed to it in those diseases for which in any case there are more certain remedies.

Potassium permanganate is a substance of considerable importance, but its action is due not to the manganese, but to its oxidising power, and is shared by other oxidising agents. It will therefore be considered with the latter.

Manganese

Mangani Chloridum (B.P.C.). 2–10 gr.
Mangani Glycerophosphas (B.P.C.). 1–5 gr.
Mangani Hypophosphis (U.S.P.). 3 gr. (200 mg.).
Mangani Peroxidum (B.P.C.).

Mangani Peroxidum Præcipitatum (B.P.C.). Mangani Dioxidum Præcipitatum (U.S.P.). 4 gr. (250 mg.).
Mangani Phosphas (B.P.C.). 1–5 gr.
Mangani Sulphas (U.S.P.). 4 gr. (250 mg.).

Bismuth.—Bismuth differs from the other heavy metals in that it is used almost entirely in the insoluble form, its action being chiefly that of an inert powder. The official compounds (oxide, carbonate, subnitrate and salicylate) are all insoluble in water. When taken internally, they may undergo certain changes in the stomach and intestine, but these do not convert them into a soluble form. Thus any of the compounds mentioned may be partly transformed into the oxychloride in the stomach, and into carbonate and sulphide in the intestine. Hence, not only are they insoluble to begin with, but, so far as they are changed, they are still insoluble. They, therefore, pass through the alimentary canal almost entirely unabsorbed, and any traces that are absorbed are too small to produce any effects.

There is, therefore, no evidence that their action is, so far as concerns the bismuth radicle, anything more than a mechanical one. They are widely used in conditions of dyspepsia and of catarrh and ulceration of the stomach. In the form of an insoluble powder, they adhere to the mucous membrane of the stomach and cover it over with a fine deposit which protects it and allays undue irritability. Possibly the bismuth may adhere rather more to an ulcerated surface than to the normal mucous membrane, and so give the former a denser coating, which protects it from irritation by food or gastric juices. In this way it tends to prevent pain and vomiting and to a less extent hæmorrhage in gastric ulcer.

Bismuth compounds exert a somewhat similar action on the intestine, coating over its surface with an insoluble deposit. In this case larger doses are naturally required. They are used in certain forms of diarrhœa, to soothe and protect the mucous membrane. No doubt they also tend mechanically to condense the watery secretion, and part of their effect is ascribed to the removal, as bismuth sulphide, of sulphuretted hydrogen which in free form augments intestinal peristalsis.

Such differences in action as are manifested by different compounds are due to differences in their acid radicles. Thus the oxide and carbonate, in addition to the mechanical action, neutralise free hydrochloric acid in the stomach, the carbonate also liberating some CO_2. The salicylate will liberate some salicylic acid, and have, in addition to the "bismuth action," an antiseptic action corresponding to the amount of acid freed. The subnitrate, which is the salt most frequently used, gives off some free nitric acid even in contact with water. This should be remembered in prescribing it and also in regard to its pharmacological action, since it exerts, in addition to a mechanical protective action, the astringent and antiseptic action of nitric acid in small amount.

The selection, therefore, of a particular salt depends upon which of these actions, additional to the mechanical one, may or may not be desired.

A solution of a soluble double citrate of bismuth and ammonium is also official. Though this solution may have a transient astringent action while the bismuth remains soluble, it is doubtful if it exerts any definite pharmacological action beyond that of the insoluble compounds, because it is precipitated both by hydrochloric acid and by carbonates, and hence will be largely, if not entirely, precipitated in the stomach and intestine.

As has been stated, none of the bismuth compounds appear to be absorbed ordinarily from the stomach or intestine in sufficient quantities to produce any effects on the tissues. Very large quantities have been given in the course of X-ray work, and, provided the intestinal mucous membrane is intact, have given rise to no symptoms pointing to the absorption of bismuth. In cases where the subnitrate has been used, a few instances have been recorded of nitrite poisoning from reduction of nitrate in the intestine. The remote effects of bismuth are, therefore, only of slight medicinal importance and have been discovered chiefly by the injection, subcutaneously or intravenously, of soluble double salts of bismuth in the lower animals. Recently, however, bismuth salts have been used as antiseptics for wounds, etc., and from raw surfaces the metal may be absorbed in sufficient quantity to cause serious symptoms, which are chiefly those of irritation of the alimentary canal—stomatitis, with a peculiar black discoloration of the mouth, vomiting, diarrhœa and nephritis—effects probably due to the excretion of bismuth by the mucous membranes involved.

Bismuth compounds are also used in the form of ointments or powders as soothing and protective applications to the skin.

Bismuthi Carbonas (B.P.). Bismuthi Subcarbonas (U.S.P.). 5–20 gr. (3–12 dqm.).
- Glycerinum Bismuthi Carbonatis (B.P.C.). 10–40 min.
- Mistura Bismuthi (B.P.C.). $\frac{1}{2}$–1 fl. oz.
- Mistura Bismuthi cum Soda (B.P.C.). $\frac{1}{2}$–1 fl. oz.
- Pasta Bismuthi (B.P.C.). 3 in 10.
- Pastillus Bismuthi (B.P.C.). 3 gr.
- Pastillus Bismuthi et Morphinæ (B.P.C.). $\frac{1}{40}$ gr. Morphine Acetate.

Pulvis Bismuthi Aromaticus (B.P.C.). 5–20 gr.
Tablettæ Bismuthi et Sodii Bicarbonatis (B.P.C.). 1–3 tablets.
Trochiscus Bismuthi Compositus (B.P.). $2\frac{1}{2}$ gr. each (0·15 gm.). 1–6 lozenges.
Unguentum Bismuthi (B.P.C.). 1 in 8.

Bismuthi Citras (U.S.P.). 2 gr. (125 mg.).

Bismuthi et Ammonii Citras (U.S.P.). 2 gr. (125 mg.).
Elixir Bismuthi (B.P.C.). $\frac{1}{2}$–1 fl. dr.
Granulæ Bismuthi et Ammonii Citratis (B.P.C.). 30–60 gr.
Liquor Bismuthi Citratis (B.P.C.). $\frac{1}{2}$–1 fl. dr.
Liquor Bismuthi Concentratus (B.P.C.). 15–30 min.
Liquor Bismuthi et Ammonii Citratis (B.P.). $\frac{1}{2}$–1 fl. dr. (2–4 mils.).
Mistura Bismuthi Composita. $\frac{1}{2}$–1 fl. dr.
Mistura Bismuthi Composita cum Morphina. $\frac{1}{2}$–1 fl. dr.
Mistura Bismuthi Composita cum Pepsino. $\frac{1}{2}$–1 fl. dr.

Bismuthi Hydroxidum. 5–20 gr.

Bismuthi Naphtholas. 10–30 gr. (0·65–2 gm.).

Bismuthi Nitras. 5–10 gr.

Bismuthi Oleas.
Unguentum Bismuthi Oleatis. 1 in 8.

Bismuthi Oxyiodidum. 5–10 gr.

Bismuthi Oxyiodogallas (Airol).

Bismuthi Phenas. 5–20 gr.

Bismuthi Salicylas (B.P.). Bismuthi Subsalicylas (U.S.P.). 5–20 gr. (0·32–1·3 grm.).

Bismuthi Subchloridum. 5–20 gr. (0·32–1·3 grm.).
Pasta Bismuthi et Zinci.

Bismuthi Subgallas (U.S.P.). Average dose 4 gr. (0·26 grm.).
Suppositoria Bismuthi et Resorcini.

Bismuthi Subnitras (B.P., U.S.P.). 5–20 gr. (0·32–1·3 grm.).
Cereoli Bismuthi et Plumbi.
Insufflatio Bismuthi et Morphinæ. Ferrier's Snuff.

Bismuthi Tannas. 10–30 gr. (0·65–2 grm.).

Cerium.—Oxalate of cerium has been used in cases of dyspepsia and vomiting, especially the vomiting of pregnancy. It is an insoluble salt and is not absorbed. It acts in the same manner as bismuth and it is doubtful if it possesses any advantages over the latter.

Cerium

Cerii Sulphocarbolas. 1–5 gr. (0·065–0·32 grm.).

Cerii Oxalas (U.S.P.). 2–10 gr. (0·13–0·66 grm.).
Granulæ Cerii Oxalatis. 30–60 gr.

Chromium.—Both chromic acid and potassium bichromate have a limited use as therapeutic agents for their local actions. Both are powerful oxidising agents and antiseptics, but are somewhat irritant. The acid is also a caustic if used in strong solution.

Potassium bichromate has been used in certain forms of dyspepsia and gastralgia in which it is given in small doses (*e. g.* $\frac{1}{8}$ gr.) well diluted before meals.

Chromium

Acidum Chromicum. Chromii Trioxidum (U.S.P.).
Gargarisma Acid Chromici. 1 in 500.
Liquor Acidi Chromici. 1 in 4.
Pigmentum Acidi Chromici. 1 in 48.

J. A. G.

PHOSPHORUS

Within the last century the position of phosphorus as a therapeutic agency has undergone many ups and downs. Considered at one time as a remedy of universal value, its applications gradually dwindled down till it was almost neglected, to be revived again within recent years in the form of the hypophosphites and glycerophosphates. The element phosphorus is a necessary constituent of nervous and bony tissues, but it is extremely difficult to be certain that the administration of the drug has any decided influence on the course of diseases of the nerves or bones. Clinical reports vary enormously, and as concomitant factors of which we have little knowledge enter in the production of improvement in such diseases it is practically impossible to make decisive statements on the therapeutics of phosphorus. In general, phosphorus has no specific action on any one tissue, it acts largely, like its two allies arsenic and antimony, on the metabolism of the body.

Chemistry of Phosphorus

Inorganic.—Phosphorus, like arsenic and antimony, is one of the elements in group V, family D, of Mendeléeff's system. It is, unlike arsenic and antimony, a typically non-metallic element. Obtained from bone-ash—pure calcium phosphate—phosphorus exists in two forms, the yellow and the red varieties. Red phosphorus differs from the yellow form in having no taste or smell, in showing no luminosity in the dark and in being quite innocuous to organisms owing to the fact that it is not absorbed. Acidum Phosphoricum (orthophosphoric acid, H_3PO_4) is prepared by the oxidation of phosphorus. Acidum Hypophosphorosum, H_3PO_2, is obtained from barium hypophosphite; and pyrophosphoric acid, $H_4P_2O_7$, by evaporation of orthophosphoric acid, as is also metaphosphoric acid, HPO_3. Salts of these acids have been employed in medicine, but all owe their action more to the presence of the metallic ion than to the presence of the phosphorus ion.

Organic Phosphorus Preparations.—Since the discovery by Hoppe-Seyler of pure lecithin or di-stearyl-lecithin in 1872 and the subsequent proof that it was decomposed into the fatty acid, glycerophosphoric acid and choline, glycerophosphoric acid and many of its salts have been used as therapeutic agents. Acidum Glycerophosphoricum, $C_3H_5(OH)_2O.PO(OH)_2$, is a dibasic acid and can be formed synthetically by heating glycerin with two-thirds of its weight of phosphoric acid. Combinations of glycerophosphates with albuminous materials have been put on the market, including lecithin itself—choline-di-stearo-glycerophosphate, which contains about 3·8 per cent. of phosphorus.

Pharmacology of Phosphorus

External.—If phosphorus be applied to the skin in the form of an ointment it is stated to have an irritant action and may give rise to sores and gangrene. This effect, however, is not a constant one. Phosphorus, although readily oxidised in air, will remain in arterial blood for days without undergoing change; similarly, its introduction subcutaneously does not lead to an inflammatory reaction; hence, it must be concluded that unless the phosphorus becomes oxidised, with subsequent formation of acid, its irritant properties are nil. Healthy animals exposed to the action of phosphorus fumes, which consist largely of the oxides of phosphorus, show no further symptoms than bronchial irritation, and although Wegner declared that in those where a tooth was broken necrosis of the jaw set in, this fact has been contradicted by many subsequent observers, and it is evident that some other factor besides the phosphorus plays an important rôle in the jaw necrosis formerly seen in match-workers.

Internally.—1. *Digestive System.*—Administration of small continuous doses of phosphorus gives rise in time to irritant symptoms, the mouth becomes dry, flatulence and headache are observed along with an uneasy feeling in the stomach. Larger doses (3 mg. or $\frac{1}{20}$ of a grain) soon by irritation produce dyspepsia, nausea and vomiting, followed by colicky pains and diarrhœa. These primary irritant effects have been ascribed to the formation of some of the acids of phosphorus in the stomach, but this is unlikely as the oxides and acids of phosphorus have very slight toxic powers. Post-mortem, in cases of poisoning, fatty degenerative changes have been observed in the mucous membrane of the stomach and intestines, particularly in the glands. This fact is probably the correct explanation of the irritant action of phosphorus in the stomach. Phosphorus is slowly absorbed in the small intestine, its absorbability being increased by the presence of fatty material and bile, in which it is easily soluble. A small amount of phosphoretted hydrogen is formed.

2. *Blood.*—After absorption, phosphorus circulates in the blood in its elementary form and increases the number of red corpuscles, but an increase in the amount of hæmoglobin does not take place, and the leucocytes are usually diminished in number. Even large doses seem to increase the number of erythrocytes, but a concomitant increase in the formation of bile pigment would lead to the conclusion that increased destruction was also occurring. The alkalinity of the blood has been found diminished in cases of poisoning owing to the formation of acid sodium phosphate. According to Araki the hæmoglobin parts with oxygen less readily under the influence of phosphorus. Again, coagulability of the blood is diminished; this appears to be a secondary effect owing to the destruction of fibrinogen. The bone marrow, according to Stockman's researches, becomes hyperæmic and an increase in the leucoblastic elements may be observed, while the fat cells become atrophied; finally, a condition of gelatinous degeneration occurs with diminution of the cellular elements.

3. *Metabolism.*—In very small doses there seems no doubt that phosphorus has a beneficial influence on metabolism by way of increasing anabolic processes, for in no other way can its effect in increasing the general nourishment and weight of young children be explained. Exact research in this matter fails, but the clinical evidence is in favour of this action, while arsenic supplies a parallel instance. Larger doses of phosphorus hinder all synthetic processes in the body, but the formation of decomposition products by autolysis is augmented. Thus it has been shown that the formation of hippuric acid in the excised kidney is diminished by the presence of phosphorus in the circulating fluid, and the same holds with regard to the formation of glycogen in the liver. The proteins of the food and of the tissues are decomposed in larger amounts with the formation of quantities of the intermediate decomposition products: leucin, tyrosin, cystin and sarcolactic acid.

The general action of phosphorus may thus be stated—

(*a*) Diminished consumption of oxygen and formation of carbon dioxide.

(*b*) Increased but imperfect carbohydrate and protein autolysis.

(*c*) Diminished fat metabolism, resulting in fatty degeneration of the tissues.

The increase in the autolysis or destructive metabolism of the carbohydrates and proteins leads to diminution of the glycogen of the liver, and one of the products of its decomposition is lactic acid. The latter diminishes the alkalinity

of the blood, increased ammonia is formed in the tissues to counteract this, and the nitrogen excretion of the urine is thus augmented. At the same time other imperfect autolytic products make their appearance in the urine, *e. g.* leucin and tyrosin, and although the urea and uric acid may be increased this is not a constant result. Hence we must assume that the increased amount of nitrogenous excretion in the urine is largely due to the ammonia consequent on the elimination of lactic acid into the blood. The urine also contains an increased amount of phosphates and sulphates resulting from the increase in katabolism. A definite increase in the power of the liver for protein metabolism has been observed by Jacoby in animals under the influence of phosphorus.

The diminished metabolism of fat and the causation of fatty degeneration of the internal organs is more difficult to explain. The fatty degeneration occurs most commonly in the liver, although it is also frequent in the kidneys, the heart and other muscles, and in the glands of the stomach and intestines. This process sets in with the appearance of cloudy swelling in the cells, then the appearance of oil droplets in the cells ensues, and finally the degenerated cells shrink and the interstitial connective tissue increases in amount until a typical cirrhosis results. The effect of these changes in the case of the liver is a swelling of the organ and the enlarged liver presses on the bile ducts, which also show cholangitis, with the result that jaundice sets in. This is further augmented by the increased formation of bile pigment from the destruction of hæmoglobin. The theory generally accepted in explanation of the fatty degeneration regards the fat as merely transported from its normal positions and redeposited in the cells of the liver, heart and kidneys, etc. This is supported by the facts that the total fat of the body is not increased, that the fat found in animals fed on foreign fats is that of the food and not of the animal itself, as it should be if the increased protein autolysis were the causal agent; and that the fat found in the liver, etc., is that characteristic of the subcutaneous tissues.

4. *Circulatory System.*—Phosphorus directly depresses the heart muscle and slows and weakens the beat. Such an effect is not observed with therapeutic, but only with large toxic doses. In chronic poisoning the weakened action of the heart is due to fatty degeneration. The smaller arteries and capillaries are affected by fatty degeneration which may lead to local œdema or hæmorrhages and perhaps gangrene. A paralysis of the peripheral endings of the vasomotor nerves such as that seen in arsenic is also stated to occur.

5. *Respiratory System.*—No marked effect is produced by phosphorus on respiration; as already stated there is a diminished intake of oxygen and a lessened excretion of carbon dioxide.

6. *Neuro-Muscular System.*—There is no evidence to show that phosphorus has any specific influence upon nerves and muscles. It has been stated to produce a general tonic effect on the capacity for exertion and work, but there is no experimental confirmation of this assertion. The foundation for its use as a nervine tonic is the fact that phosphorus is a component of nervous matter.

7. *Genito-Urinary System.*—In chronic phosphorus poisoning albuminuria is not an uncommon symptom, while fatty casts may be present; these are no doubt sequelæ of the fatty degeneration. As already noted, leucin, tyrosin and sarcolactic acid may be found in the urine, which is often increased in amount. The former idea that phosphorus acted as an aphrodisiac has not been substantiated.

8. *Osseous System.*—The formation of bony tissue is markedly influenced by phosphorus. In young animals the spongy tissue of the epiphyses is replaced by compact bone and the shaft of long bones also increases at the expense of the medullary cavity. This effect is seen not only in the long bones, but also in the ribs, vertebræ, wrists and ankle bones and in the pelvis. If the phosphorus administration be continued, the cartilage of the epiphyses of the long bones becomes bony tissue and the cancellous tissue becomes absorbed, with the result that the medullary cavity increases in size. Microscopically the structure of the new bone is characteristic of that tissue; the Haversian canals are narrower, so that the bone is more compact, but they do not become obliterated; thickening of the periosteum is also observed. These effects have been referred to a stimulation of the osteoblasts, and certainly they indicate a preponderance of anabolic over katabolic processes. If, however, calcium be withheld from the organism, Wegner, on whose work these statements are founded, discovered that the same processes resulted, but the bone deprived of the calcium resembled that of rickets. The changes may, perhaps, be explained on another basis: that of the retention of calcium. It has been shown in animals treated by phosphorus that the percentage of calcium increases in the bones from 21 per cent. to 25 per cent., and Schabad has found that in rickety children treated with phosphorus there is more calcium absorbed and less excreted in the urine and fæces; this calcium retention occurs within three to five days of commencing phosphorus treatment, and if phosphorus be discontinued the excretion of calcium again increases to normal. It was found that in

healthy children the calcium excretion was not interfered with. These results indicate rather that there is increased absorption with diminished calcium metabolism present during phosphorus administration, but it is probable that both factors play their part in producing the specific action.

9. *Excretion of Phosphorus.*—Phosphorus may pass through the alimentary canal unchanged, but the great proportion is absorbed and excreted in the urine as phosphates. A small portion is excreted by the lungs.

Pharmacology of the Hypophosphites.—The hypophosphites were introduced into medicine by Dr. J. F. Churchill in 1857; he believed they were specifics for tuberculosis. They are readily absorbed and can be almost quantitatively recovered in the urine unchanged. There is no direct evidence that they are of any value, but they are stated to improve appetite and digestion and lessen the expectoration of phthisis.

Pharmacology of the Glycerophosphates.—These have been introduced into therapy since it was discovered that they formed one of the decomposition products of lecithin, which has also been employed. Danilewski and Serona both found that lecithin exerted a favourable influence on growth and metabolism, the appetite and nitrogenous metabolism being increased and the number of erythrocytes augmented. It is, however, improbable that they are of more value than phosphorus and the phosphates.

Therapeutics of Phosphorus

The therapeutical value of phosphorus and its preparations is confined to the formation of bone and the treatment of nervous disorders. Small doses are believed to act as digestive tonics. Such small action as may be exerted must be ascribed to their irritant effect.

Diseases of Bone.—Continental experience was formerly strongly in favour of the use of phosphorus in the treatment of rickets, but whether the "English illness" differed from the Continental type or not, equally beneficial results have not been obtained in this country. Nowadays the majority of Continental writers are agreed that phosphorus is not the panacea for rickets which it was supposed to be. It is, however, worthy of trial, and the consensus of opinion is in favour of the Elixir Phosphori as the best preparation; this may be combined with cod-liver oil, which latter may itself produce the improvements that are observed, although cases are on record in which relapse has occurred on phosphorus being omitted. Others advise a two-hundredth of a grain of phosphorus in thirty minims of cod-liver oil thrice daily. The use of calcium hypophosphite, and especially calcium glycerophosphate, has been stated to produce beneficial results. Where good effects have occurred from the administration of phosphorus in rickets the observers have noted not only improvement in the bone development, but also a diminution of the rickety cachexia, in the lessened emaciation, increased subcutaneous fat and the disappearance of the abdominal distension; at the same time the laryngismus stridulus seems to be efficiently cured by phosphorus administration. Lecithin, nucleinate of soda and phytin, and other organic phosphorus preparations have all been tried in the treatment of rickets. The results on the whole are not encouraging.

In osteomalacia phosphorus seems occasionally to be of service; it should be administered early and be kept up for months if any benefit is to be obtained.

Blood Diseases.—Phosphorus has been tried in cases of pernicious anæmia, leucocythæmia and lymphadenoma, but without producing any marked influence on the course of these diseases in the opinion of most observers.

Nervous Diseases.—Phosphorus has long been vaunted as a specific in nervous debility in its various forms. Several authorities are of the opinion that the general nutrition is improved through the influence of the drug on the nervous system, and the glycerophosphates and acid glycerophosphates are stated to give tone to the nervous system, but, contrary to these statements, there is no direct evidence that the nervous system makes use of glycerophosphoric acid to regenerate fresh nervous tissue. Danilewski believes with regard to lecithin that it acts as a nervine stimulant, augmenting assimilation and the cerebral functions. The general results of treatment with the glycerophosphates and lecithin show a close likeness to the metabolic changes seen with small doses of phosphorus. A solution of yolk of egg, which is rich in lecithin, in oil of sweet almonds has been given hypodermically in neurasthenia, with, it is stated, benefit.

On the whole phosphorus cannot be said to be of great value in the treatment of nervous diseases; it may be tried in neurasthenia, neuralgia and the nervous debility common in the present age, but good and nourishing diet with fresh air and exercise will probably produce just as beneficial influence on the course of these troubles.

Respiratory Diseases.—The use of phosphorus preparations—hypophosphites and glycerophosphates—in phthisis can only be considered palliative; they may be tried along with more active forms of treatment as they are said to increase the appetite, diminish expectoration and cough. No reliance should, however, be placed on them as curative principles.

Toxicology of Phosphorus

Acute.—No symptoms as a rule appear for some hours after taking a toxic dose of phosphorus. They commence with pain and burning in the stomach, garlic eructations, and, finally, vomiting of material with the odour of garlic and with the property of exhibiting luminosity in the dark; the vomiting may be frequently repeated, and bile appear in the vomited material. Usually, however, these symptoms disappear and the patient remains two or three days in almost usual health, to develop anew symptoms of general phosphorus poisoning. Pain in the stomach and tenderness of the whole abdomen with vomiting, often blood-stained, occur, followed by diarrhœa. The liver increases in size, becomes tender, and jaundice appears. Pains in the limbs, headache and weakness, with a feeble pulse, are common, and hæmorrhages may occur in the bowel, nose and under the skin. Death follows from collapse and coma. Occasionally, after a huge dose, death follows very rapidly; this may be due to direct paralysis of the heart muscle.

Post-mortem.—The skin may show an icteric tint, and small petechial hæmorrhages may be found under the skin, in mucous membranes and in the internal organs. The stomach and intestinal mucous membrane is yellowish in appearance, small erosions may be seen, and the epithelium is in a state of fatty degeneration. The liver is enlarged from fatty degeneration, and similar degenerative changes may be found in the spleen, heart and kidneys.

Fatal Dose—varies from one to five grains.

Fatal Period—may be as short as twelve hours and seldom extends beyond a week.

Chronic Poisoning.—The principal characteristic symptom of chronic phosphorus poisoning is the occurrence of necrosis of the bones of the jaw. The pathology of this condition is unsettled, but the probabilities are in favour of the view that the inhalation of phosphorus fumes may induce a latent sclerosis of the bone with stimulation of the bone-forming cells, and that tuberculous infection occurring by way of carious teeth is the principal factor in the production of the necrosis. Short of the production of jaw necrosis, continued inhalation or ingestion of phosphorus leads to general weakness and anæmia, with slight jaundice, and frequently causes gastric catarrh and enteritis with diarrhœa as a symptom. The commencement of bone trouble is usually observed by an inflammation of the gum of the lower jaw and its separation from the alveolar process. Periostitis of the bone then occurs, and finally goes on to actual necrosis, which may spread from the original site along the bone. Although the lower jaw is most commonly the seat of the infection, other bones have been observed to undergo similar changes.

Treatment of Poisoning.—*Acute.*—1. Give emetics, wash out the stomach and administer a purgative; avoid administering oils and fatty material in which phosphorus is soluble.

2. Administer copper sulphate, two- or three-grain doses dissolved in water, every five minutes till vomiting occurs, and thereafter in grain doses every quarter of an hour; the copper sulphate is reduced and a coating of copper formed on the surface of the phosphorus.

3. The stomach should be washed out with potassium permanganate solutions 0·2 per cent. several times in order to oxidise the phosphorus still remaining. Hydrogen peroxide, 1 to 3 per cent., is also used, but is of less value.

4. After the immediate treatment, the administration of old oil of turpentine in half-drachm doses, three times a day, has been advised, but has proved useless. The administration of alkaline remedies is employed to increase the alkalinity of the blood.

5. When symptoms reappear and the patient tends to pass into coma, administer saline solution, alkaline with sodium bicarbonate, intravenously to counteract the lessened alkalinity of the blood.

Chronic.—1. Remove the cause of poisoning.

2. Treat cachexia with tonics.

3. Surgical treatment for the jaw necrosis.

Detection of Phosphorus

Should a large quantity of phosphorus have been taken the vomited matters will show luminosity in the dark due to oxidation occurring. Where smaller doses have been taken the vomited material is distilled in a flask in a dark room, with the addition of a little tartaric acid. The phosphorus vapour is carried through a narrow glass tube to a Liebig's condenser. As distillation continues, the phosphorus vapour, driven off, comes in contact with air in the narrow tube and a luminous flickering ring becomes apparent. The presence of alcohol disturbs the delicacy of the test.

Preparations of Phosphorus

1. Phosphorus (B.P., U.S.P.). Characters, semi-transparent wax-like, solid, luminous in the dark, insoluble in water.
   Dose: $\frac{1}{100}-\frac{1}{25}$ gr. (0·6–2·5 mg.).
   (*a*) Oleum Phosphoratum (B.P.). 1 per cent. phosphorus in almond oil.
   Dose: 1–5 min. (6–30 cl.).
   (*b*) Pilula Phosphori (B.P., U.S.P.). 1 per cent. phosphorus in oil of theobroma and kaolin.
   Dose: 1–4 gr. (6–25 cg.).
   (*c*) Sevum Phosphoratum (B.P.C.). 1 in 10.
   Dose: $\frac{1}{10}-\frac{1}{2}$ gr. (6–30 mg.).

(*d*) Pilulæ Phosphori cum Quinina (B.P.C.). Each pill contains $\frac{1}{5}$ gr. of phosphorated suet, and 1 gr. of quinine sulphate.
Dose : 1–2 pills.
(*e*) Pilulæ Phosphori Compositæ (B.P.C.). Each pill contains $\frac{1}{10}$ gr. of phosphorated suet, $\frac{1}{4}$ gr. quinine sulphate, $1\frac{1}{2}$ gr. reduced iron, and $\frac{1}{100}$ gr. strychnine.
Dose : 1–2 pills.
(*f*) Tinctura Phosphori Composita (B.P.C.). Contains 0·2 per cent. phosphorus in chloroform and alcohol.
Dose : 3–12 min. (2–7 dl.).
(*g*) Elixir Phosphori (B.P.C.). Compound tincture of phosphorus in glycerine. Each fluid drachm contains $\frac{1}{50}$ gr. phosphorus.
Dose : 15–60 min. (1–4 ml.). The best method of giving phosphorus.
(*h*) Elixir Phosphori Compositum (B.P.C.). Compound tincture of phosphorus with oil of anise, glycerin and aromatic elixir. Each fluid drachm contains $\frac{1}{50}$ gr. phosphorus.
Dose : 15–60 min. (1–4 ml.).

2. Acidum Hypophosphorosum (U.S.P.), H_3PO_2. Characters, colourless, odourless, acid liquid.
Dose : 2–5 min. (12–30 cl.).
(*a*) Acidum Hypophosphorosum Dilutum (U.S.P.). Contains 30 per cent. of acidum hypophosphorosum.
Dose : 5–15 min. (3–10 dl.).

3. Sodii Hypophosphis (B.P., U.S.P.). $NaPH_2O_2$. Characters, white granular deliquescent salt, with bitter taste.
Dose : 3–10 gr. (2–6 dl.).
(*a*) Syrupus Sodii Hypophosphitis (B.P.C.).
Dose : 1–4 fl. dr. (4–16 ml.).

4. Potassii Hypophosphis (U.S.P.). KPH_2O_2. Characters, white deliquescent hexagonal plates.
Dose : 1–5 gr. (6–30 cg.).

5. Calcii Hypophosphis (B.P., U.S.P.). $Ca(PH_2O_2)_2$. Characters, white pearly crystals, with bitter taste, soluble in water.
Dose : 3–10 gr. (2–6 dg.).
(*a*) Glycerinum Hypophosphitum Compositum (B.P.C.). Contains calcium, manganese, potassium, iron and quinine hypophosphites, with $\frac{1}{80}$ gr. strychnine in each fluid drachm.
Dose : 1–2 fl. dr. (4–8 ml.).
(*b*) Pulvis Hypophosphitum Compositus (B.P.C.). Composition as Syr. Hypophos. Co.
Dose : 1–4 gr. (6–25 cg.).
(*c*) Syrupus Calcii Hypophosphitis (B.P.C.).
Dose : 1–4 fl. dr. (4–16 ml.).
(*d*) Syrupus Hypophosphitum Compositus (B P.C.). Contains calcium, potassium, manganese, iron and quinine hypophosphites, with $\frac{1}{160}$ gr. strychnine in each fluid drachm.
Dose : 1–2 fl. dr. (4–8 ml.).
(*e*) Syrupus Hypophosphitum (U.S.P.). Contains hypophosphites but no strychnine.
Dose : 2 fl. dr. (8 ml.).

6. Magnesii Hypophosphis (B.P.C.). $Mg(H_2PO_2)_2,6H_2O$. Characters, white crystals, soluble in water.
Dose : 3–10 gr. (2–6 dg.).

7. Barii Hypophosphis (B.P.C.). $Ba(H_2PO_2)_2$. Characters, white crystals, soluble in water.
Dose : $\frac{1}{4}$–1 gr. (16–60 mg.).

8. Ferri Hypophosphis (U.S.P). $Fe(PH_2O_2)_3$. Characters, whitish amorphous powder, slightly soluble in water.
Dose : 1–3 gr. (6–20 cg.).
(*a*) Liquor Ferri Hypophosphitis Fortis (B.P.C.).
Dose : 10–30 min. (6–18 dl.).
(*b*) Syrupus Ferri Hypophosphitis (B.P.C.).
Dose : $\frac{1}{2}$–2 fl. dr. (2–8 ml.).

9. Mangani Hypophosphis (U.S.P.). $Mn(PH_2O_2)_2$, H_2O. Characters, white or rose-coloured crystals, soluble in water.
Dose : 1–6 gr. (6–40 cg.).

10. Quininæ Hypophosphis (B.P.C.). $C_{20}H_{24}N_2O_2HPH_2O_2$. Characters, colourless small prisms, slightly soluble in water.
Dose : 1–5 gr. (6–30 cg.).

11. Acidum Glycerophosphoricum (B.P.C.). $C_3H_5(OH)_2OPO(OH)_2$. Characters, clear, colourless, odourless liquid with acid taste.
Dose : 5–10 min. (3–6 dl.).

12. Calcii Glycerophosphas (B.P.C.). $CaC_3H_5(OH)_2PO_4$. Characters, crystalline leaflets or powder, soluble in water.
Dose : 3–10 gr. (2–6 dg.).
(*a*) Granulæ Calcii Glycerophosphatis (B.P.C.).
Dose : 30–60 gr. (2–4 g.).
(*b*) Glycerinum Glycerophosphatum Compositum (B.P.C.). Contains calcium, potassium, sodium, magnesium and iron glycerophosphates, with no sugar.
Dose : 1–2 fl. dr. (4–8 ml.).
(*c*) Glycerinum Glycerophosphatum cum Medulla Rubra (B.P.C.).
Dose : 1–2 fl. dr. (4–8 ml.).
(*d*) Pulvis Glycerophosphatum Compositus (B.P.C.). Contains calcium, magnesium and iron glycerophosphates with nux vomica and pepsin.
Dose : 5–10 gr. (3–6 dg.).

(*e*) Syrupus Glycerophosphatum (B.P.C.). Contains calcium, potassium, sodium, magnesium and iron glycerophosphates with caffeine and sugar.
Dose: 1–2 fl. dr. (4–8 ml.).

(*f*) Syrupus Glycerophosphatum Compositus (B.P.C.). Contains in addition to above $\frac{1}{80}$ gr. strychnine in each fluid drachm.
Dose: 1–2 fl. dr. (4–8 ml.).

(*g*) Syrupus Glycerophosphatum cum Formatibus (B.P.C.). Contains the above with sodium and potassium formates and $\frac{1}{80}$ gr. strychnine in each fluid drachm.
Dose: 1–2 fl. dr. (4–8 ml.).

13. Sodii Glycerophosphas (B.P.C.). $Na_2C_3H_5(OH)_2PO_4H_2O$. Characters, yellowish crystalline masses, soluble in water.
Dose: 5–10 gr. (3–6 dg.).

14. Potassii Glycerophosphas (B.P.C.). $K_2C_3H_5(OH)_2PO_4$. Characters, yellow or brown amorphous masses, soluble in water.
Dose: 5–10 gr. (3–6 dg.).

15. Lithii Glycerophosphas (B.P.C.). $Li_2C_3H_5(OH)_2PO_4$. Characters, white crystalline powder, soluble in water.
Dose: 8–15 gr. (5–10 dg.).

16. Magnesii Glycerophosphas (B.P.C.). $MgC_3H_5(OH)_2PO_4$. Characters, white amorphous powder, soluble in water.
Dose: 5–10 gr. (3–6 dg.).

17. Ferri Glycerophosphas (B.P.C.). $FeC_3H_5(OH)_2PO_4$. Characters, yellowish powder or scales, slightly soluble in water.
Dose: 1–5 gr. (6–30 cg.).

18. Mangani Glycerophosphas (B.P.C.). $MnC_3H_5(OH)_2PO_4$. Characters, white amorphous powder, soluble in water.
Dose: 1–5 gr. (6–30 cg.).

19. Quininæ Glycerophosphas (B.P.C.). $(C_{20}H_{24}N_2O_2)_2C_3H_5(OH)_2H_2PO_4,4H_2O$. Characters, crystalline, odourless bitter powder, slightly soluble in water.
Dose: 1–10 gr. (6–60 cg.).

20. Lecithinum (B.P.C.). Characters, brownish or yellowish translucent waxy mass, swells up but does not dissolve in water, soluble in chloroform, ether, alcohol and fixed oils.
Dose: 3–8 gr. (2–5 dg.).

(*a*) Elixir Lecithini (B.P.C.). 1 gr. in 1 fl. dr.
Dose: 1–4 fl. dr. (4–16 ml.).

(*b*) Emulsio Lecithini (B.P.C.). 1 gr. in 1 fl. dr.
Dose: 1–4 fl. dr. (4–16 ml.).

(*c*) Glycerinum Lecithini (B.B.C.). 1 gr. in 1 fl. dr.
Dose: 1–4 fl. dr. (4–16 ml.).

(*d*) Pilulæ Lecithini (B.P.C.). Each contains $1\frac{1}{2}$ gr. lecithin, and $\frac{1}{80}$ gr. strychnine hydrochloride.
Dose: 1–4 pills.

21. Calcii Lactophosphas (B.P.C.). Characters, white hygroscopic crystalline powder.
Dose: 3–8 gr. (2–5 dg.).

(*a*) Syrupus Calcii Lactophosphatis (B.P.).
Dose: $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

(*b*) Syrupus Calcii Lactophosphatis cum Ferro (B.P.C.).
Dose: $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

22. Magnesii Lactophosphas (B.P.C.). Characters, white powder, soluble in water.
Dose: 3–15 gr. (2–10 dg.).

23. Zinci Phosphidum (B.P.C.). Zn_3P_2. Characters, dark grey, minute crystalline fragments, of metallic lustre, insoluble in water.
Dose: $\frac{1}{20}$ – $\frac{1}{4}$ gr. (3–16 mg.). (*Obsolete.*)

W. J. D.

ARSENIC

Preparations of arsenic as toxic agents have been known from early historical times, for example, the yellow sulphide of arsenic was known to Dioscorides as ἀρσενικόν, and it was also used in Arab and Hindu medicine; again, arsenical preparations formed the bases of many of the secret poisons employed in the Middle Ages. The metal arsenic is in itself non-poisonous on account of its insolubility, which permits of its passage through the alimentary canal unchanged. The characteristic poisonous and pharmacological actions are due to the dissociation of the negative ion, AsO_3, which is typically represented in the molecule of arsenious acid, H_3AsO_3. Any limitation of the dissociation of this ion diminishes the toxicity of the respective arsenical compound; thus, arsenic acid and arsenates are less toxic than arsenious acid and arsenites, while the cacodylates, in which the arsenic ion is intimately bound up with the aliphatic radical, pass through the body almost unchanged and without appreciably influencing it. The aromatic organic compounds probably owe their prolonged activity to the slow dissociation of the arsenic ion in the body tissues from its combination with the aromatic nucleus. Arsenic is a powerfully toxic substance, but it does not affect all organisms in the same degree; thus the aim of chemo-therapy in recent years has been directed towards the attainment of a substance which shall be powerfully toxic towards parasites (parasitotrop), and only slightly, or not at all, toxic towards the organism or host (organotrop).

Chemistry of Arsenic

Inorganic.—Arsenic forms one of the five elements in Group V, Family B, of Mendeléeff's

system, the members of the group being nitrogen, phosphorus, arsenic, antimony and bismuth. These show a gradual transition from non-metal to metal, and arsenic, which stands on the border-line, is chemically a "metalloid."

Pure arsenic, prepared by heating arsenical pyrites, $FeAs,FeS_2$, in earthen tubes and subliming, is a brittle crystalline metal of a steel-grey colour; when heated, it sublimes, giving a white vapour having a garlic-like odour. An amorphous dark-brown, and a yellow form resembling yellow phosphorous in its solubility in carbon bisulphide and its luminosity in the dark from oxidation, are known as allotropes. There are two oxides of arsenic: arsenious oxide, $(As_2O_3)_2$—so-called acidum arseniosum—which sublimes in the form of regular octahedra, and arsenic oxide, As_2O_5, to which correspond the acids, arsenious acid, H_3AsO_3, and arsenic acid, H_3AsO_4. From arsenious acid, which is not known in the free condition, are derived the "arsenites" such as copper hydrogen arsenite or Scheele's green, $HCuAsO_3$, a poisonous pigment, and the pigment known as Schweinfurter or Paris green is a double metarsenite and acetate of copper. Arsenious acid is more toxic than arsenic acid and, according to Husemann, their relative toxicity is as two is to one.

Arseniuretted hydrogen is formed during the generation of hydrogen or carbon dioxide if a soluble compound of arsenic be present in the materials; it was formerly a frequent source of poisoning from the use of impure products in the various arts. The salts of arsenic acid are those most commonly employed in medicine, for example, ferrous arsenate, sodium arsenate.

Organic Compounds. — Nomenclature. — The following terms are generally accepted as marks of distinction between different organic arsenical compounds.

Arsonic Acid indicates a derivative of arsenic acid, $AsO(OH)_3$, in which one hydroxyl has been replaced by an organic radical. Salts of this acid are termed arsonates.

Arsinic Acid implies a derivative of arsenic acid, $AsO(OH)_3$, in which two hydroxyls have been replaced by organic radicals, *e. g.* cacodylic acid. On the Continent these terms are not distinguished.

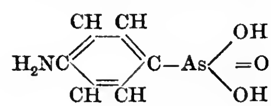
Arylarsonate is an aromatic arsonate in which the radical substituting hydroxyl is of an aromatic nature.

Arseno- is a term affixed to denote that the two arsenic atoms are coupled together by a double bond, *e. g.* arseno-benzene, $C_6H_5\text{-}As = As\text{-}C_6H_5$.

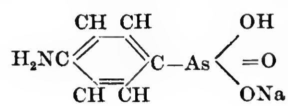
The Aliphatic Series of Compounds. — The arsenic compounds belonging to the aliphatic series consist largely of the cacodylates. Cacodyl, or tetramethyl-diarsine, $(CH_3)_2As\text{-}As(CH_3)_2$, was discovered by Bunsen in 1842. Cacodylic acid or dimethyl-arsinic acid, $(CH_3)_2AsO,OH$, is an oxidation product of cacodyl. Pharmacologically it is practically inert, as the arsenic ion undergoes almost no appreciable dissociation in the body. The various cacodylates, sodium, ferric, magnesium, quinine, strychnine, etc., are derivatives of cacodylic acid; like their parent substance they are relatively non-toxic, and undergo little ionic dissociation in the body.

"New Cacodyle," arrhenal or monomethyl-sodium arsonate, $CH_3Na_2AsO(OH)_2$, is, for similar reasons to those above stated, of limited pharmacological importance. Other aliphatic compounds of arsenic have been prepared, but they have not fulfilled expectations as useful remedies.

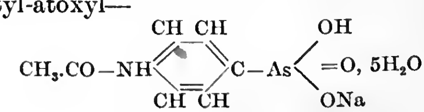
Aromatic Arsenic Compounds.—The aromatic series is primarily derived from compounds of arsenic with the benzene ring-nucleus, and is allied in constitution to the nitro- and azo-benzenes, etc.; thus we have arsino-benzene, $C_6H_5.AsO_2$, and arseno-benzene, $C_6H_5.As = As.C_6H_5$. But the first of the aromatic arsenic series to attract attention was atoxyl. This was prepared by Béchamp by heating arsenic acid with anilin, which forms anilin arsenate, and this, by prolonged heating at 190° C., forms p-aminophenylarsonic acid—



as was proved by Ehrlich and Bertheim, and the sodium salt of this compound, obtained by extraction with sodium carbonate and re-crystallising, forms atoxyl—

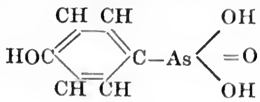


The acid is commonly termed arsanilic acid and the sodium salt sodium arsanilate. The corresponding acetyl derivative, termed arsacetin or acetyl-atoxyl—

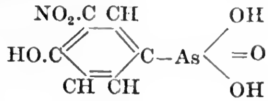


which is less toxic than atoxyl, and the sodium methylacetyl - p - amino - phenyl arsonate or "orsudan" have also been introduced for therapeutic purposes. The chemical processes for the transition from atoxyl to salvarsan are protected by patents; they may be summarised thus: By reduction of arsanilic acid, diamido-arseno-benzol $H_2N.C_6H_4As = AsC_6H_4NH_2$ can be obtained direct, but in actual practice the

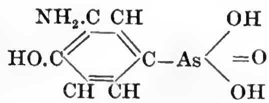
transition to salvarsan is attained by replacing its amino group by hydroxyl, when the body p-oxyphenylarsonic acid is formed—



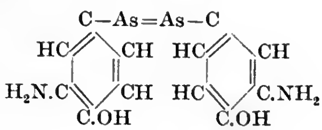
This is nitrated by a mixture of sulphuric acid and nitric acid, and the resulting nitrophenylarsonic acid—



is then reduced by sodium amalgam to aminophenylarsonic acid—



This substance on further reduction with sodium sulphide forms by combination of two molecules, dioxydiamino-arseno-benzol—



which base is converted into the hydrochloride.

Neosalvarsan, a descendant of the parent substance, is sodium-dioxydiamido-arseno-benzol-mono-methano-sulphonate,

$$C_{12}H_{11}O_2As_2N_2.CH_2O.SONa,$$

and consists of a yellowish powder, easily soluble in water, with neutral reaction.

Many other aromatic compounds of arsenic have been prepared, of which space will not permit description.

Pharmacology of Arsenic

General.—Arsenious oxide, or anhydride, As_4O_6, is the most characteristic arsenical preparation, and in discussing the pharmacology of the substance its action is that of which we shall mainly treat. As mentioned above, it owes its action to the dissociation of the negative ion, AsO_3, from its watery solutions which contain the hitherto unisolated arsenious acid, H_3AsO_3. Arsenic oxide and its corresponding salts, the arsenates, are less toxic than arsenious acid and the arsenites in the proportion of 2 to 1, while they contain arsenic respectively in the proportion of 3 to 2. This diminished activity is due, no doubt, to the lessened dissociation of the toxic ion, a statement borne out by the fact that the stable cacodylates are relatively inactive. The cacodylates do not undergo dissociation in solution, and therefore pass through the system and are excreted in the urine largely in an unchanged condition. Such dissociation as occurs results in the formation of cacodyl, which is excreted in the breath, giving it an alliaceous odour, and a small percentage is perhaps oxidised, from which arsenic is set free in ionic form to exert its typical effects. Similarly, atoxyl, which is forty times less toxic than arsenious acid, is eliminated largely unchanged in the urine, but a small amount is decomposed by the tissues, and this provides the all-important arsenic ion. Finally, the toxic action which these bodies, and especially salvarsan, exert towards parasites must be capable of explanation on the same basis. It is known that certain algæ, *e. g.* Penicillium brevicaule, have the power of forming poisonous gaseous products from arsenical preparations, thus we may assume it to be probable that the parasites of sleeping sickness and syphilis possess power also to decompose arsenical compounds, and that they bring about their own death by setting free from a compound relatively innocuous to the host, small quantities of arsenic in ionic form which is highly toxic towards themselves.

External Actions.—Arsenic is a fairly powerful antiseptic, being about one-tenth as strong as mercuric chloride, but its high toxicity precludes its use for this purpose in practice. It produces these effects through its specific toxic properties, and not by the precipitation of protein material. Its antiseptic properties are put to use in the arts for the preservation of animal and vegetable tissues, such as the preparation of skins in taxidermy, in the dissecting-room, etc. Towards certain of the pathogenic protozoa arsenic has a more specific action, trypanosomes are destroyed by concentrations as weak as 1 to 200,000 although other protozoa will survive in much stronger solutions. Arsenic has little or no effect on ferment activity, thus it does not interfere with the action of pepsin; indeed, in very dilute solutions, arsenic, like most antiseptics, seems to promote fermentative action.

Arsenic is powerfully irritant and caustic, but on the unbroken skin it has no effect; it is not dissolved by fatty material, and is, therefore, not absorbed by the integument, except in those who are arsenical workers, in whom the arsenical material may collect about the hands, scrotum, etc., where it ultimately becomes dissolved in the sebaceous secretion and produces inflammation and ulceration with consequent absorption of the arsenic from the raw surface. If applied to a raw surface the irritant properties of arsenic are fully developed; there results an inflammatory reaction with subsequent exudation, blistering, and finally

necrosis of the tissues, which separate in the form of a slough in about three to four weeks, leaving below a cicatrix. This action is accompanied by great pain, but it is seldom that toxic symptoms occur from the absorption of the arsenic, owing to its simultaneous destruction of the blood-vessels and lymph-channels. This holds only for strong concentrations of arsenic which produce circumscribed death of the tissues; weaker solutions are readily absorbed from raw surfaces, and have given rise to fatal poisoning. These caustic effects are not exerted on the dead subject, and are to be ascribed to the specific toxic properties of arsenic on living tissues; the action is naturally greater on unhealthy ill-nourished tissues.

Internal Actions. 1. *Digestive System.*—Small doses of arsenious anhydride taken repeatedly have the power of stimulating appetite: this effect may be due to a slight irritant action exerted by the drug on the mucous membrane of the stomach; it results in a feeling of warmth in the organ, improvement of appetite and general invigoration. Arsenic causes no interference with the digestive ferments, and as it does not precipitate proteins, it has no deleterious influence on the digestive processes. If given in full medicinal doses, however, it is apt to set up irritation of the mouth, followed by salivation and the appearance of a silvery coating on the tongue, which later may become red and distinctly inflamed. Should the dose be persisted with, similar effects result in the stomach and intestines, ushered in by pain, sickness and diarrhœa. In such circumstances, the mucous membrane of the stomach is found red and swollen, either in patches or distributed uniformly throughout the organ. Occasionally actual hæmorrhages may be seen, and the mucous membrane is in an extremely friable condition. These effects are strongly reminiscent of corrosive poisoning, but arsenic does not influence protein, and, further, the fact that similar appearances are elicited by the subcutaneous injection of arsenic precludes the idea that the action is a strictly local one. Comparable appearances to the above are found in the intestine, the mucous membrane being congested and in some places eroded—especially in the neighbourhood of the agminated glands—so that the contents of the bowel are a thin watery fluid containing portions of exfoliated mucous membrane.

These actions appear to be explainable only on the supposition of a specific action of arsenic on the walls of the alimentary canal, and although it does not explain all the circumstances there is sufficient evidence to support this theory. Thus, if the affected mucous membrane be examined microscopically, many of the epithelial cells are found to have vanished, those remaining have undergone cloudy swelling and, in later stages, fatty degeneration, while the interstitial tissue is invaded by granular cells. Boehm and others explain this on the ground that arsenic produces a paralysis of the nerve centres, and later of the arterial and capillary muscle, with the result that finally the intestinal vessels do not react to stimulation of the splanchnic nerves. This paralysis of the contractility of the mesenteric capillaries, which results in their dilatation and a condition of blood stasis, is followed by transudation of fluid below the epithelium, which has already undergone fatty degeneration by a specific and selective action of the arsenic. The final stage is reached by the exfoliation of the degenerated epithelium and the exudation of the watery fluid into the intestine.

Therefore, while small doses of arsenic are beneficial to the intestinal mucosa, either by exerting on it a mildly irritant action or by the above specific effect on the epithelium, large doses are deleterious, and the symptoms above described are to be avoided.

2. *Blood.*—Arsenical preparations are absorbed readily from the mucous membrane of the alimentary canal; the form in which absorption takes place is not definitely known, but in the absence of evidence that combination occurs between arsenic and proteins we must assume that the arsenic is absorbed in the form in which it is administered. After reaching the blood the arsenic appears to be carried largely by the polynuclear leucocytes, and ultimately reaches the liver, which acts as a storehouse for the greater portion of it.

The pharmacological action of arsenic on the blood has long been disputed, and is at present by no means settled. Generally speaking, it is believed that small doses of arsenic lead to an increase in the number of erythrocytes, but this is not conclusively settled. Stockman and Greig concluded that in a healthy animal no increase could be ascribed to the number of red or white corpuscles nor to the amount of hæmoglobin; by administering large doses of arsenic they found that, instead of increase, an actual decrease in the number of corpuscles and hæmoglobin content ensued. Nevertheless, after hæmorrhage and in pernicious anæmia, competent observers have described a decided increase in the number of corpuscular elements after the administration of arsenic. These facts are not extraordinary, since we are aware that in the healthy organism it is extremely difficult to augment the number of blood corpuscles. According to several authorities, the action of arsenic consists in promoting an increase in the number of nucleated red cells while diminishing the number of erythrocytes, but from the experiments of Stockman and

Greig arsenic has no appreciable action in increasing the number of erythroblasts, and there is no evidence of increased corpuscular destruction as is exemplified by the absence of an increase in the iron pigment in the spleen, liver, etc.

The bone marrow is certainly profoundly affected, from small doses there ensues an increase in the number of leucoblastic cells, marked hyperæmia, and atrophy of the fat cells, but no visible increase in the number of erythroblasts. The increase of the leucoblastic elements is probably a protective attempt on the part of the organism to deal with the poison. Large doses, on the other hand, cause hyaline degeneration of the bone marrow. Stockman, therefore, feels compelled to assume that the beneficial effect of arsenic in pernicious anæmia, etc., is not due to a specific action on the blood, but to its antidotal effect on the causal agency of the disease. The inhalation of very small quantities of arseniuretted hydrogen produces rapid hæmolysis, and large quantities cause complete decomposition of the blood pigment, but in very weak dilutions—1 in 400,000—Gunn found that arsenious acid renders the red corpuscles less susceptible to the hæmolytic action of distilled water.

3. *Metabolism.*—Arsenical preparations have an undoubted influence on the metabolism of the body, and in this way arsenic has acquired its reputation as a general tonic. These metabolic effects are presumed to be due to the diminished oxidising power of the tissue cells induced by the arsenic, a theory readily acceptable since a diminution of oxygen pressure leads to increase of metabolism. Binz and Schulz ascribed the action to an alternate withdrawal and supply of oxygen produced by the oxidation of arsenious to arsenic acid and its subsequent reduction again. This theory will not bear the test of the evidence, but whatever the ultimate cause, arsenic has an indubitable influence on nutrition.

Under small doses there is an increase of the assimilation processes concomitant with a decrease in katabolism, and thus the body weight increases. This is accompanied by improved digestion and appetite, the subcutaneous and mesenteric fat increases in amount, the general bodily vigour is augmented, and the respiratory function is improved. The nitrogenous metabolism appears to be diminished, but exact information as to the total metabolism is wanting. It would seem that while assimilation is greater, owing to improved digestion, there is a slight decrease in the nitrogenous excretion even in the fæces. A stimulation also occurs in the bone marrow, and, according to Gies, the bones of rabbits treated with arsenic are longer, thicker and the epiphyses more compact than those of normal animals. The arsenic animals also showed a more rapid growth than control animals, they exhibited greater activity, and in female animals treated with arsenic the young were larger and heavier than normal. The nutrition of the skin is also improved.

Under large doses the reverse effects are obtained, nitrogenous metabolism is increased, as is shown by the loss in weight and the augmented excretion of nitrogenous substances in the urine. This increase may affect the urea, but undoubtedly there is excessive excretion of ammonia. The glycogen is diminished and may even disappear entirely, since the liver appears to lose its power of converting sugar into glycogen. There is an increased formation of lactic acid, which, passing into the blood stream, lowers its alkalinity, and is ultimately detectable in the urine. A diminution occurs also in the gas exchanges and the blood corpuscles undergo degeneration, and death results from severe anæmia. Concomitantly fatty degeneration occurs in various organs throughout the body, thus the liver becomes enlarged, the parenchymatous cells are seen in a condition of active division, and even necrotic patches have been noted. The pressure of the enlarged liver on the bile ducts, together with cholangitis, prevent the escape of bile, and jaundice, accompanied by the excretion in the urine of bile acids and pigment, results. The kidneys, muscle cells of the heart and blood-vessels, the striated muscles and the alveolar epithelium in the lungs are also affected by fatty changes.

There is little doubt that under varying dosage and circumstances these two actions—the favourable and unfavourable—may go on side by side in the body, depending on the concentration of the arsenic ions in the respective organs.

4. *Circulatory System.*—Therapeutic doses of arsenic do not affect the circulatory system to any marked degree, the increase in force and frequency of the heart occasionally observed being secondary to the general functional improvement. In the frog's heart arsenic causes the beats to become slow and weak, and ultimately the heart stops in diastole from a direct muscular paralysis. In mammals the most marked action is a large fall of blood pressure due to a dilatation of the small arteries, principally in the splanchnic area.

5. *Respiratory System.*—Arsenic has little influence on the respiratory function, small doses have been asserted to act as respiratory stimulants by an action on the respiratory centre and also on the vagus terminations, as shown by the fact that section of the vagi, although it diminishes, does not annul the effect.

The Styrian peasants, however, believe that arsenic renders respiration easier, less laboured and less hurried under exertion. This may be explained on the basis of its power in reducing the oxygen consumption of the tissues.

6. *Neuro-Muscular System.*—The action of arsenic on nervous tissues has been the subject of considerable dispute. Ringer and Murrell found that in frogs arsenic caused a definite paralysis of all nervous tissues, beginning in the brain, then affecting the spinal medulla, and lastly the motor-nerve terminations. These symptoms are not observed in man, with whom death occurs before any nervous symptoms have developed. By the administration of continuous maximal doses, peripheral neuritis may be induced.

7. *Skin, Mucous Membranes and Glands.*—As already indicated, metabolic changes occur also in the skin; these consist in an accelerated growth and increased proliferation of the epithelium; at the same time, the epidermal nutrition is improved, the subcutaneous fat increases, and the complexion becomes clearer; the skin is usually increased in thickness. In frogs a hypodermic injection of arsenic results in a ready peeling of the cuticle in a few hours, which effect is due to a degeneration of the deepest layer of epidermal cells. In mammals the gloss of the hairy coat is improved. These are the results of small doses, but larger doses give rise to skin eruptions of a papular or scaly type; pigmentation of the skin (bronzing or arsenic melanosis) on the abdomen, breast, face, and other parts of the body, may occur, while falling off of hair and defective nutrition of the nails is occasionally observed.

The explanation of the effects is by no means simple. They cannot be due to local vascular dilatation such as occurs in the intestine, since there is no evidence of rise of temperature. Arsenic, however, is quite definitely excreted by the skin, and probably by the sweat glands, thus we may postulate a specific local action of arsenic on epithelial structures, although it is possible that the flow of lymph to the part is increased, which would also explain the results.

Acting on mucous membranes, arsenic increases the secretion and is itself excreted by them. Inflammatory reactions, such as redness of the lips, nose and throat, conjunctiva and urethra, are not uncommonly observed. Chronic naso-pharyngeal catarrh and a congested appearance of the conjunctiva accompanied by itching should be warnings that the therapeutic dose has been exceeded.

The secretion of many glands is also augmented by small doses of arsenic; for example, it increases the sweat secretion, and an actual diaphoretic action has been ascribed to it. Increase in the urinary secretion has also been observed, and a doubtful cholagogue action is said to exist.

8. *Action on Parasites.*—It has been pointed out above that arsenic has antiseptic properties, and that the reason of its inapplicability for this purpose is its very toxic properties towards higher as well as lower organisms. Researches on chemo-therapy by Ehrlich and his co-workers have recently been directed towards the production of some compound of arsenic which shall be highly toxic to parasites (Parasitotrop) and feebly toxic to higher organisms (Organotrop). It has been found that organisms acquire a tolerance to repeated doses of arsenic, this led Ehrlich to strive after the attainment of a parasitotropic drug, which when given in sufficient dose would result in a rapid and total destruction of the parasites infecting the host. This is the basis of his "Therapia sterilisans magna," which has not yet been realised.

By investigating the relative toxicity of various arsenical compounds for parasites and host, a series of new bodies has been formed, all tending in their action towards increased parasitotropism and diminished organotropism. The fundamental facts which admitted of the investigations are these: Towards protozoal parasites in a test-tube, arsenious acid and such organic arsenical compounds as are analogous to it in containing the trivalent arsenic radical, As_2O_3, are powerfully toxic, whereas this toxic property is possessed to a much less degree by the corresponding derivatives of the pentavalent arsenic oxide, As_2O_5. To this pentavalent group belong atoxyl and arsacetin, and just as arsenic acid probably produces its action by a reduction in the body to arsenious acid, so these relatively non-toxic organic products effect their results by a partial decomposition of the pentavalent arsenic radical to the trivalent condition; but if by the action of reducing agents atoxyl is converted into the body p-amidophenylarsen oxide, this latter substance (As trivalent) kills trypanosomes in strengths of 1 : 500,000 in three minutes and of 1 : 100,000 immediately. Ehrlich has suggested that the trypanosomes possess an "arsenoceptor" or "arsenoreceptor" element which combines with the arsenic compound and brings the two into close combination, resulting in the reduction of the arsenic and the death of the parasite. The action of atoxyl in destroying the trypanosomes of sleeping sickness was discovered by Thomas of Liverpool in 1905, and Koch demonstrated that it abolished the parasites from the blood and the lymph glands. In 1906 its action was tried on syphilis, and although favourable results were obtained these did not fulfil the hopes of their investigators as the dose required for therapy

was dangerously near the toxic and led to optic atrophy. The favourable results from atoxyl led to a series of investigations along the lines above indicated, and there were produced arsacetin—less toxic than atoxyl and as powerfully parasitotropic, but liable to cause untoward symptoms; atoxylate of mercury—which had much of the good effects of the first two with fewer untoward symptoms; hectine—which never came into general use, and others. Ehrlich now concluded that the excessive organotropic action of atoxyl, etc., was due to the presence of the pentavalent arsenical radical. By reduction he endeavoured to obtain a substance containing the arsenic in trivalent condition—arsenophenylglycin; this he found was strongly parasitotropic both for sleeping sickness and syphilis, but secondary effects of a toxic nature led to its being abandoned. Finally, towards the end of 1909, Ehrlich announced the discovery of salvarsan, which, while powerfully parasitotropic, showed very small organotropic effects.

Action of Salvarsan on Parasitic Diseases.—The administration of salvarsan in mice infected with the spirillum of relapsing fever resulted in cure with a single dose, and similar curative effects were obtained by Hata in the spirillosis of fowls. Experiments made by Hata on spirilla of relapsing fever indicated that salvarsan had little toxic power on them in vitro; thus, concentrations of 1 : 4000 were necessary to render them immobile, but spirilla which had been subjected to dilutions up to 1 : 100,000 have less power of producing the disease than those in control experiments, thus they lose their power of regeneration under the influence of salvarsan. In syphilis of rabbits curative results were obtained in very large chancres by one dose, and on the day following the injection the organisms were found to have disappeared. Comparable, if less remarkable, results were obtained in apes infected with the syphilitic virus. In man symptoms of cure set in very early and the spirochætes mostly disappear at the end of a day from the manifestations of the disease, and those still detectable at the end of two days are swollen and altered in appearance, although in isolated cases they may persist longer. They disappear from the glands in the course of three to five days after an injection. As a criterion of its power in abolishing the syphilitic virus from the blood, the Wassermann reaction may be taken. Nevertheless, the results of this reaction must be viewed with a critical eye, since, as McDonagh has pointed out, a single injection was considered curative originally because the reaction was negative at the end of two months, and in some primary cases having originally a negative reaction there developed a positive reaction within two days or at most a week after the injection, and this returned to negative again in two months. Later, however, these cases developed recurrences with a reappearance of the positive reaction; hence, during the negative phase, the patient could only be considered as being in a latent stage. Ehrlich considers the permanent absence of the positive Wassermann reaction as evidence of cure, but, except in very early primary conditions, this is unlikely to be attained by a single dose. McDonagh has shown that by repeated injections of salvarsan the Wassermann reaction can be permanently abolished. Cases also exist which have been treated with mercury and show no Wassermann reaction, but which, on administering an injection of salvarsan, develop a positive reaction, and the same holds for women who, while showing no symptoms themselves, give birth to syphilitic children. In such instances the disease is merely in a latent condition. McDonagh therefore concludes that three to seven injections are necessary to obtain a cure of syphilis, and that even after a uniform negative Wassermann reaction has been obtained it is advisable to administer, six months or a year later, another injection in the endeavour to provoke a positive reaction if there be traces of syphilitic virus still remaining. Should the action remain negative, complete cure may be considered to have resulted.

Regarding the action of salvarsan, Ehrlich believes that it kills the spirochætes, and that the dead organisms liberate a protein which stimulates the formation of a syphilitic anti-body. There are several grounds to support this view—thus, healing continues after the whole of the salvarsan has apparently been excreted, the serum of patients treated with salvarsan has curative powers, etc.; and in para-syphilitic cases where spirochætes are few, salvarsan has less effect, due on this hypothesis to absence of the anti-body formed by the destruction of the spirochætes. McDonagh considers that the spirochæta is merely the adult male of the syphilitic parasite and that the activity of salvarsan in the early stages of the disease is due to its toxic action on the spores of the parasite.

General Pharmacological Effects of Salvarsan.—Oral and rectal administrations have no marked effect. Intramuscular and subcutaneous injections give rise as a rule to considerable pain, and in most cases a febrile reaction ensues. This latter has been ascribed by McIntosh and others to the use of saline solutions which are not microbe-free, the toxic effects being due to the dead microbes themselves and not to their toxins. Even under the best laboratory conditions, large doses of salvarsan cause toxic

symptoms, the most marked being gastric inflammation and hæmorrhage and enteritis; the fevers and rigors occurring in secondary syphilis may be due to endotoxins. In the blood salvarsan causes a moderate leucocytosis; the increase is largely in the polymorphonuclears, although the eosinophiles have also been found augmented. The red corpuscles are first diminished and then increased in number, and occasionally jaundice has been seen with the presence of bile pigment in the urine. Salvarsan appears to cause a fall in the blood pressure, but this is by no means a marked feature of its action and is of no more importance than that characteristic of arsenic itself. Its administration is followed by improvement in the general health, and it appears to reach even the corneal tissue and, according to some writers, is excreted in the milk, though others deny this. Not uncommonly, rashes and other untoward symptoms appear after salvarsan injections, they set in after a considerable interval, which is shortened after re-injections, especially if these are given in rapid succession, facts which do not agree with the theory of anaphylaxis. It is probable that they are due to liberation of arsenic and the development of an acquired idiosyncrasy. The composition of the cerebro-spinal fluid has been recorded as altered, but this statement was contradicted by Wechselmann, who found no evidence of the effects of salvarsan in the nervous system. Nevertheless, fatal epileptiform cases have been observed, and in one case histological examination of the brain showed the presence of stasis, hyaline capillary degeneration and punctiform hæmorrhages, which changes, however, might probably have been due to the syphilitic virus.

According to Alt, the excretion of arsenic, when administered intravenously, is almost complete at the end of two days, although other observers extend the period to eight days or even up to one month. Given intramuscularly, the excretion lasts twelve to thirteen days or longer. After all trace has disappeared from the blood, its presence can still be demonstrated in the liver and other organs.

9. *Tolerance of Arsenic.*—If animals or human subjects have administered to them gradually increasing doses of arsenic, they acquire in time an immunity to the drug, so that they can ingest many times the lethal dose without ill-effects. The best-known example of this is the enormous doses used by the Styrian mountain peasantry. But the peasants, on taking a dose of arsenic, refrain from drinking for some time afterwards, which may delay its rapid absorption. The immunity acquired appears to hold only for administration by mouth, and to be much more marked in the case of solid than fluid preparations, for Cloetta found that animals rendered immune by arsenical food developed typical gastro-intestinal symptoms and were rapidly poisoned by an injection of arsenic. He concluded that the secret of the immunity lay in a greater resistance by the alimentary tract to the absorption of arsenic; this is supported by the fact that as tolerance increases, less arsenic is excreted in the urine and more in the fæces. Moreover, those exposed to the dust of arsenical ores do not exhibit immunity to injection. Nevertheless, evidence has been adduced that the serum of an arsenic-immune animal has antitoxic powers towards arsenic, and that an injection of arsenic into the peritoneal cavity is less toxic than hypodermic administration. It is possible that the leucocytes which do ingest arsenic may possess the power of fixing it in some harmless organic form.

10. *Excretion of Arsenic.*—Arsenious anhydride is slowly and probably incompletely excreted, the largest proportion is got rid of by the fæces, a smaller portion passes into the urine, while a still large remainder cannot be recovered. It appears to be stored in the bones for considerable periods, and a slow excretion proceeds by way of the skin long after the urine and fæces are free from it. After its administration it disappears rapidly from the blood, and excretion begins in about twenty-four hours. Arsenic administered by hypodermic injection is excreted mostly in the urine.

Therapeutics of Arsenic

Methods of Administration.—1.—Official Preparations.—All arsenical preparations having irritant effects on the gastro-intestinal tract should be administered well diluted and immediately after meals, so that the food may act as a further diluent. Further, the preliminary doses should be small and gradually increased as the patient can stand them. Children are remarkably tolerant of arsenic, and can usually be given doses suitable for adults from the fifth year onwards. Where a combination of iron and arsenic is desired, it is best administered as a pill. Ferri Arsenas is not a salt to be recommended in such cases as the quantity of iron it contains in a dose is so small.

2. **New Organic Preparations.**—Cacodylic acid and its derivatives have been administered by the mouth, per rectum, and by hypodermic injection. It has been shown, however, that they are relatively inert bodies, and their value is limited. Of those belonging to the aromatic series, atoxyl has been given by the mouth, 4–20 cg. ($\frac{3}{4}$–3 gr.) and by intramuscular injection, the site selected being the gluteal region (2–6 dg. or 3–10 gr. in 10 per cent. solution); 50 per cent. ointments have been advised as

local treatment in syphilis. The German Commission on sleeping sickness recommended subcutaneous injection of two doses of 0·4 gm. on successive days, repeated every tenth or eleventh day. Other members of this series are administered by similar methods.

3. **Salvarsan.**—In early salvarsan therapy subcutaneous and muscular injections were employed, and many modifications were suggested to avoid the pain and necrosis which occurred at the seat of injection. Neutral watery suspensions were found to cause less pain than the original alkaline solutions. Oily suspensions of the drug were also employed with some success. The present method of employing the drug is by intravenous injection, which is practically painless, and if correct technique be followed no local infiltration develops round the puncture. Many firms supply apparatus for the performance of intravenous injection; these are not indispensable, and are merely useful adjuncts in the attainment of success. Generally speaking, the technique is as follows—

Preparation of the Solution.—Salvarsan is supplied as the acid hydrochloride in sealed glass tubes. For intravenous injection it must be converted into the alkaline salt. The glass tube containing the required quantity of salvarsan is scratched with a file and sterilised externally by alcohol. The tube is broken and the substance poured on the top of 30–40 c.c. of sterile freshly distilled water contained in a sterile graduated glass-stoppered cylinder of about 300 c.c. capacity. By vigorous shaking the salvarsan passes into solution, and to this, when it is absolutely clear, is added from a sterile burette or pipette a solution of sodium hydrate till the neutral point is reached (with a normal sodium hydrate solution 0·1 gm. salvarsan requires approximately 0·7 c.c. of soda solution). The addition of the alkali causes a precipitate to form, which re-dissolves on shaking. Excessive alkalinity may be diminished by cautious addition of acetic acid solution 10 per cent. The clear yellow solution is now diluted with sterile hypotonic saline solution (about 0·5 per cent. is recommended), prepared from chemically pure sodium chloride and distilled water, or with sterile distilled water, until each decigram of salvarsan is dissolved in 40–50 c.c. of fluid, *e. g.* for 0·5 gm. salvarsan 250 c.c. fluid. If the solution be not quite clear a drop at a time of soda solution should be added and the solution shaken till turbidity disappears. The solution is finally warmed to about 37° C.

Preparation of Patient.—The patient should receive a purgative the evening before, and no food should be given on the morning of the injection. The injection must be given with the patient recumbent, and this posture should be adopted for at least twenty-four hours succeeding the injection; solid food is best avoided for three to four hours after injection, lest sickness occur. A vein in the forearm or at the elbow is selected; by the application of a bandage to the arm it is rendered more prominent; and the skin over it is scrubbed with some antiseptic.

Apparatus.—The necessary apparatus consists of a suitable sterilisable syringe and needle, but most observers find that a syringe with a three-way stop-cock is an advantage, allowing as it does of the fluid being sucked up from the cylinder and injected without removing the syringe from its position; the introduction of a small glass tube connected by rubber between the needle and syringe is also of value in rendering any air bubbles detectable before they have gone too far.

Method of Operation.—The needle, which should be of medium size, is run in almost parallel to the skin, so as to enter the vein but not puncture its deep wall. In order to make certain as to the position of the needle, the syringe should first be filled with sterile saline and some of this allowed to flow into the vein. If no swelling occurs the syringe may now be filled with the salvarsan solution and the fluid slowly injected. The time taken for a complete injection should be from five to ten minutes, and at the end of the process a small quantity of saline should be allowed to run in so as to wash the needle free of salvarsan. On removing the needle the puncture may be sealed with collodion.

Very many workers much prefer to make use of some form of gravitation method of administration, and of both methods there are many varieties of apparatus in the market.

Dosage.—The usual intravenous dosage in healthy adults is for men 0·4 to 0·6 gm. (6–9 gr.), for women 0·3 to 0·4 gm. (4½–6 gr.), and in enfeebled patients the dose should be diminished and repeated if well tolerated.

Neosalvarsan.—Neosalvarsan may be given intramuscularly or intravenously by the same methods as salvarsan. Neosalvarsan, being soluble in water with neutral reaction, requires no previous treatment. For intramuscular use a 5 per cent. solution in distilled water is employed, an injection of novocain being given previously to allay pain and, for intravenous administration, 0·15 gm. should be dissolved in about 25 c.c. of freshly distilled water or 0·4 to 0·5 per cent. of pure saline solution. Solutions must be freshly prepared, and should not be warmed above 20 to 22° C. (68 to 71° F.). The average dosage is for males 0·6 to 0·9 gm., for females 0·45 to 0·6 gm.

Combination of Salvarsan or Neosalvarsan with

Mercury.—Increasing evidence of the inefficacy of salvarsan to produce a complete cure of syphilis has led to the adoption of a combined treatment with salvarsan and mercury ointment by inunction or mercury cream by injection. The following course of treatment is that adopted at the Royal Army Medical College: Three injections of salvarsan 0·6 gm. (or 0·9 gm. of neosalvarsan) are given at intervals of six weeks, and during each interval weekly injections of five minims (containing one grain of mercury) of Adams's mercurial cream are given. This routine has given excellent results in respect of cure and freedom from relapses.

Therapeutical Uses of Arsenical Preparations

External.—Arsenical preparations made into pastes, plasters, etc., have been employed as caustics for the treatment of lupus, cancerous ulceration and similar growths. The destruction which occurs is gradual and painful, and the dry slough separates in about a fortnight. Arsenic is not a suitable caustic, and its use is, or should be, obsolete. Arsenical pastes and wool are still employed in dentistry for the destruction of nerves, but it is very desirable that this method should be discontinued in favour of the more satisfactory one of pressure anæsthesia. The arsenic is liable to penetrate the dentine and cementum and set up periostitis. In nearly all cases its use is attended with excessive pain.

Internal. 1. *Digestive Disorders.*—Preparations of arsenic have proved of value in the treatment of many gastro-intestinal troubles; thus, in convalescence from severe illness, where digestion is weak and appetite diminished, arsenic is a valuable remedy in stimulating the digestive functions to regain their normal activity, and in irritative dyspepsia and gastralgia it is a useful gastric tonic given in small doses in solution after meals. It has been found beneficial in various chronic forms of vomiting such as that of alcoholism and pregnancy, while cases of chronic dyspepsia, associated with general weakness, flatulence and acidity, are markedly benefited by its administration. In soluble form it has also been advised for the treatment of gastro-enteritis and the diarrhœa of children, and is particularly useful in cases where diarrhœa comes on during or shortly after meals. Sodii Arsenas is somewhat less irritant than arsenious acid and its solutions and is therefore preferable in the treatment of digestive disorders; but in any case arsenic should not be given for long periods or in large doses, as it readily tends to cause gastric irritation.

2. *Diseases of the Blood.*—In simple anæmias and chlorosis the value of arsenic as a blood-forming medium is disputed. Several writers have made authoritative statements to the effect that arsenic does increase the corpuscular elements in simple anæmias, but a consensus of opinion in the matter has never been attained. The effect, if any, must be slight, and is explainable by the general improvement in nutrition. The administration of iron and arsenic in combination for anæmia is, however, a most satisfactory method of treatment. It has been stated that arsenic has the power of increasing the absorption of iron.

In pernicious anæmia administration of arsenic undoubtedly produces an increase in the erythrocytes and in the amount of hæmoglobin, the patient improves under its influence and seems on the road to recovery. Relapses, however, always occur, and arsenic, although it is the only remedy which is of much service, is by no means curative. For leukæmia the same statements hold good, during a time at least arsenic improves the condition of the sufferer, the red cells increase in number, concomitant with a diminution of the white cells and a reduction in the size of the liver and spleen, but in spite of continued treatment the cases ultimately retrogress. Hodgkin's disease or lymphadenoma has been benefited and in some cases it is said even cured by arsenic; a start should be made with five minims of the Liq. Arsenicalis three times daily, and this should be increased up to fifteen minims and even further if it can be tolerated. Arsenic has been injected into the glands in this condition with benefit, and subcutaneous injection of Liq. Arsenicalis has been recorded as curative in at least one instance, but these results are by no means constant.

Arsenic is the only other drug, except quinine, which has a marked influence on malaria, but it is of much less value in acute cases. It has decided prophylactic effects and is advisable in malaria cases which show an idiosyncrasy to quinine or in which quinine has lost its effects.

3. *Metabolic Diseases.*—In diabetes arsenic has been advised probably on account of the fact that glycosuria does not occur after puncture of the medulla oblongata (puncture diabetes) in animals poisoned by arsenic, but in such animals curare and other drugs still elicit glycosuria. The results of treatment have been discouraging, and it is not to be recommended as a remedy, although writers have stated that it is of value when given after the sugar has been reduced by dieting and codeine. The cacodylates have also been tried in diabetes with a negative result.

Certain cases of chronic rheumatoid arthritis may exhibit improvement under arsenical treatment, and the remedy is worthy of trial

in this resistant condition. Arsenical baths containing 15 to 30 gr. of sodium arsenate have been recommended. The treatment is only palliative, but even then it is worth a trial, which should be one of months not days. Whether its effect is due to the action of arsenic on bony tissue or not is undetermined. It may be of some value in the treatment of rickets.

4. *Circulatory Diseases.*—The administration of arsenic has been recommended in various circulatory disorders such as angina pectoris, cardiac weakness, amenorrhœa, etc. While benefit may be obtained by its use there is no evidence to show that it is of superior value to the remedies which would ordinarily be prescribed in such conditions.

5. *Respiratory Diseases.*—At one time arsenic was considered a suitable remedy for consumption; this, however, has not stood the test of time, and such effect as is produced is of a general tonic character. At the recent (1913) International Medical Congress, Dr. Chavant of Grenoble exhibited an apparatus for the administration of arsenical vapours by inhalation; he stated that the treatment is curative in early, in some advanced cases, and in tuberculous laryngitis. He uses a dose per day corresponding to 18 mg. of arsenic given at ten or more sittings. He claims to have obtained about 75 per cent. of cures in all cases treated by this method. Further reports must be awaited before the value of arsenic in tuberculosis can be conclusively determined.

It has been found of benefit in asthma, in which disease cigarettes containing sodium arsenate ($\frac{3}{4}$ gr.) have produced relief. It acts best in cases of spasmodic asthma of a neurotic type. Asthmatical paroxysms have been allayed by the subcutaneous injection of Liq. Arsenicalis, and curative results have been obtained by continuous arsenical treatment for some months. Hay fever has also been relieved by arsenic.

6. *Nervous Diseases.*—Arsenic is a useful remedy in chorea, but requires to be exhibited in large doses; it is not a specific. It has also proved of some value in epilepsy; Arsenii Bromidum gives good results in this disease without the necessity of increasing the dose. Arsenical preparations are often of benefit in various functional neuroses, such as headache, neuralgia, migraine, neurasthenia, hysteria and nervousness in children.

7. *Skin Diseases.*—Probably arsenic is employed most largely in the treatment of cutaneous troubles; but its indiscriminate use has sometimes led to its being discredited for any skin disease. Arsenic is not a suitable remedy for eczematous conditions, nor is it a useful drug in acne. Much advantage may be gained from it in cases of pemphigus, hydroa, and in bullous conditions generally, more especially where there is an underlying neurotic condition, and it is also of service in post-herpetic neuralgia. In psoriasis arsenic often does harm in recent cases by aggravating the disease, but in old cases it frequently causes great improvement. Given in increasing doses it brings about amelioration in lichen planus. To summarise, arsenic is more likely to prove useful in the chronic and subacute forms of skin diseases than in conditions where active disease is in progress. Given along with bromides, it prevents the symptoms of bromism, and in bromide acne is decidedly curative.

8. *Parasitic Diseases.*—As long ago as 1906, successful experiments in the treatment of syphilis were carried out with atoxyl. It was found useful in all forms of the disease and was comparatively rapid in action; the doses necessary, however, were so nearly toxic that treatment was rightly suspended. Arsacetin gave similar results, but had also to be abandoned owing to the frequent occurrence of optic atrophy. Atoxylate of mercury was a more useful remedy, but the results were inconstant.

The introduction of salvarsan led to a new era in the treatment of syphilis. Originally Ehrlich believed that single injections were curative; this has not been found to be the case, and repeated injections are necessary until the Wassermann reaction becomes permanently negative (see under *Treatment of Syphilis*). Simultaneous and continuous treatment with mercury during the intervals between injections is advantageous in keeping up the treatment.

Salvarsan in the Treatment of Syphilis.—In the first place, early diagnosis is of paramount importance; when the spirochæta pallida has obtained a hold on the system, treatment becomes much more difficult and prolonged. Any suspicious genital sore should be subjected to thorough inspection; a droplet of serum obtained from its margin should be examined microscopically and, if spirochætes be found, treatment should be begun at once. If no spirochætes be found and suspicion still attaches to the sore, an injection of 0·2 gm. salvarsan is indicated to provoke a Wassermann reaction for diagnostic purposes; should it become positive, treatment must be started. The Wassermann reaction alone is of no diagnostic value in early cases, it does not become positive often till the third or fourth week after infection.

As a preliminary to treatment the primary sore should be destroyed either by excision, which is best, by cauterisation, or by calomel ointment. Single injections of salvarsan are of no further value than in curing symptoms; for curative results repeated doses of salvarsan must be given or a course of combined salvarsan and mercurial injections. All cases after treatment must be carefully watched for relapses, and

cure must not be taken for granted till there is a total absence of clinical symptoms and serological reactions, the latter also after a provocative injection of 0·2 gm. of salvarsan.

Salvarsan should be administered with great care in cases suffering from heart or pulmonary disease or in diseases of the nervous system. Patients suffering from albuminuria require careful watching, and in all such cases a smaller dose of salvarsan (0·2) should be tried and repeated at the end of a week if no untoward symptoms arise. Under proper precautions alarming symptoms and death are rare.

Theoretically a full dose of salvarsan destroys all spirochætes which can be reached by the circulation, but the process of healing sets free those which were encysted in infiltrated areas, and this takes a few weeks.

The therapy of syphilis by salvarsan may be summed up in these statements: First, early treatment is productive of the best results. Second, repeated injections of salvarsan or neosalvarsan are necessary to procure a cure; according to McDonagh, from three to seven injections at intervals of eight days or longer are indicated in individual cases: or, in primary cases three to five injections at intervals of four to seven days of 0·3–0·5 gm. salvarsan with mercury treatment for a year; in secondary cases six to nine injections with mercury for two years; and in tertiary cases sufficient injections to relieve symptoms. Third, repeated injections of salvarsan or neosalvarsan combined with injections of mercury form, according to Gibbard and Harrison the most satisfactory method of treatment, their course of administration being an intravenous injection of 0·6 gm. salvarsan, five weekly injections of mercurial cream, a second intravenous injection of 0·6 gm. salvarsan, five more mercurial injections, and finally an intravenous injection of 0·6 gm. salvarsan. Fourth, no cure can be regarded to have taken place until the Wassermann reaction is permanently negative, even after a provocative injection of 0·2 gm. salvarsan.

Primary Syphilis.—The results of treatment by salvarsan have in general been no less than startling; thus, primary lesions are often healed in a matter of a fortnight, while the induration lasts somewhat longer in many instances; in particular, indurated chancres are somewhat resistant to treatment, owing, no doubt, to deficient blood supply. With regard to local glandular enlargements, these are in many cases favourably influenced, but often they do not disappear altogether. Evidence of cure in primary cases is exhibited by the fact that re-infection has occurred.

Secondary Syphilis.—In secondary syphilis good results are observed with salvarsan, although the percentage of refractory cases is somewhat greater. Mucous lesions of the mouth and throat yield very rapidly to salvarsan, and disappear in two or three days after the injection; even a few hours after, the patient may feel relief in swallowing; the hyperæmia of the pharynx and enlargement of the tonsils also vanishes and the hoarseness of the voice clears. The secondary syphilitic rashes are usually cured, papulous and pustulous syphilides clear up and lichenoid cases are benefited. Large papulous rashes and some forms of specific psoriasis are more obstinate. Leucoplakia appears to remain uninfluenced, and often, although the various rashes heal, the characteristic copper colour of the subjacent tissues remains. The anæmia of secondary syphilis is improved by salvarsan, the headaches disappear and the general health of the patient is beneficially influenced. Any general lymphadenitis, as well as isolated enlarged glands, tends to disappear in a few days. Sometimes immediately after salvarsan has been given, exacerbation of the disease occurs.

Tertiary Disease.—Salvarsan is probably found to be more effective in tertiary disease than in any other form. In patients suffering from severe tertiary ulceration which resists the action of iodine, it often produces a general recovery, the ulcers heal, the lesions of the nasal septum improve and the fœtor of ozœna gradually disappears; therewith the patient's weight increases. Similarly in ulcerations and subcutaneous gummata very rapid absorption has been noted and gummatous infiltrations of the nose, pharynx and tongue are much improved. Good results have also been reported in cerebral syphilis.

Malignant Syphilis is, according to most observers, favourably influenced by salvarsan, although relapses have been recorded.

Ocular Symptoms.—Syphilitic iritis is, as a rule, improved, and in many cases a complete cure results; keratitis is also benefited. Choroidal and retinal exudative conditions have been favourably influenced, but in optic nerve atrophy benefit is not common.

Parasyphilitic Conditions.—Unfortunately these conditions are little affected by salvarsan unless in very early cases. The first reports of its value in tabes have not been confirmed, and in cases of tabes and general paralysis where favourable results have been obtained the improvement is temporary only. Those who have seen good results in tabes state that salvarsan relieves the lightning pains and improves sensation, speech, ataxy and the condition of the bladder. But the reflexes are usually unaffected. A new method of giving salvarsan in these affections has been introduced by Swift and Ellis. An intravenous injection of salvarsan or neo-

salvarsan is given, and an hour later the patient is bled and the serum prepared. The serum is heated to 60 C., and then diluted with normal saline previous to injection into the vertebral canal by lumbar puncture. Emery believes that the activity of the serum is due to minute traces of salvarsan and not to the presence of antibodies. Ravaut gives 6–9 mg. neosalvarsan in 0·6 % solution intrathecally and 0·45 gm. intravenously; the solvent being distilled water. The results of treatment by this method, few as the cases are, have been encouraging, the mental condition of paralytics has improved, and in tabes, complete abolition of lightning pains occurs, while the light reflex has been noted to return.

Congenital Syphilis. — The injection of salvarsan into syphilitic infants must be done with care; it is often dangerous, since, as Wechselmann states, the amount of endotoxins liberated must be huge. Nevertheless good results have been obtained in cases where it has been used, but the child to be treated should be strong. Administration of salvarsan to syphilitic women while pregnant or nursing has been productive of marked benefit to the child.

Salvarsan in other Diseases.—Beneficial effects have been obtained by the use of salvarsan in malaria, yaws, frambœsia, leprosy, glanders and pernicious anæmia, but in view of the few cases which have been recorded, judgment must be still withheld for a short time.

Neosalvarsan. — Neosalvarsan has exactly similar effects to salvarsan, and the foregoing description may be taken as applying to both; it more frequently causes toxic rashes. Its advantage is its solubility in water with neutral reaction, its disadvantage that its solutions cannot be heated lest they decompose, hence it is less likely to be of value in tropical climates.

Arsenic in Sleeping Sickness. — Atoxyl was originally thought to be a specific in sleeping sickness, but it is not curative in any degree. The most that can be said for it is that its immediate effects are good and the patient's condition is temporarily relieved. Better results were obtained with arsacetin, but in both the danger of blindness from toxic optic atrophy is too great to permit of its extended use. The exhibition of atoxyl, orsudan or soamin alternating with mercurial treatment has proved of value. These remedies cause a disappearance of the trypanosomes from the blood, but these reappear even in the course of treatment, as the parasite seems to acquire a tolerance to the drug.

Toxicology of Arsenic

Acute Poisoning.—Arsenious acid has no taste, but on account of its insolubility it frequently floats on the surface of fluids in which it may be administered. The symptoms of poisoning after a large dose arise in from half to one hour, and may be resolved into two groups: (1) in which the gastro-intestinal symptoms predominate, and (2) where paralysis of the central nervous system and heart occur. In the first form there is a feeling of œsophageal constriction, vomiting with nausea, and pain and tenderness over the stomach; great thirst and a raw feeling in the mouth and throat; and later pain and tenesmus in the abdomen followed by diarrhœa, the stools being of the "rice-water" variety. In the nervous form the characteristic symptoms are: Giddiness, headache, pains in the limbs, low blood pressure, weak irregular pulse, cyanosis, collapse, general clonic or tonic convulsions, and finally paralysis.

Post-mortem.—The body is often shrunken and the skin cyanosed, the stomach and intestines are intensely inflamed, depending on the interval between administration and death. The mucous membrane is red and like velvet, submucous hæmorrhages are often visible and epithelial erosion is common, while, if the arsenic has been taken as a solid, particles of arsenious acid are often found adhering to the walls of the stomach.

Fatal Dose—1–6 dg. (2–10 gr.).

Fatal Period.—This is extremely variable; large doses have killed in a few hours, but often death does not occur for several days.

Chronic Poisoning.—Chronic arsenical poisoning usually sets in with digestive disturbances, loss of appetite, pain in the stomach after food, nausea and tendency to vomiting, the vomited matter being slimy in character; slight and persistent diarrhœa is also an early symptom. Later, these symptoms become more acute, colicky pains develop, a feeling of soreness in the mouth and redness of the mucous membrane of the throat appear, the tongue being usually coated with a silvery fur. From the excretion of the poison irritation of the nasal mucous membrane arises, causing a persistent catarrh; and redness of the conjunctiva, especially of the lower eyelid, is a prominent symptom. Weakness of the heart and tachycardia are observed and enlargement of the liver with jaundice is common, while arsenical "diabetes" may also form a symptom. Sooner or later the skin becomes affected, excessive sweating, falling of hair, and scaling of the skin occur, and a darkening of the skin leading to arsenical melanosis soon makes its appearance. These cutaneous symptoms are commonly seen on the abdomen, the axillæ, popliteal fossæ and between the thighs. Finally the poison attacks the nervous system. Multiple peripheral neuritis may follow. Headaches, incapacity for work, with sensory and motor disturbances, such as

tingling, numbness, paræsthesia, diminution of sensibility and inco-ordination of movement giving rise to ataxy and even epileptiform attacks, are advanced symptoms. Finally, a condition of severe cachexia results.

Treatment. — Acute Poisoning. — 1. Give an emetic, either apomorphine subcutaneously, or mustard and water.

2. Administer freshly precipitated ferric hydroxide or Antidotum Arsenicum, which contains ferric hydroxide and magnesia. In emergency ferric hydroxide may be prepared by the addition to the solution of one ounce of Tr. Ferri Perchlor. in a tumblerful of water of two tablespoonfuls of sodium carbonate (washing soda); the precipitate is filtered off and given in hot water. Unlimited quantities may be given.

3. Wash out the stomach thoroughly. The ferric hydroxide precipitates the arsenic, but the insoluble salt must be removed and, if necessary, the process should be repeated. Administer castor oil or some other purgative.

4. In absence of the above remedies give magnesia, chalk or lime water and mucilaginous drinks.

5. Should prostration arise, give stimulants and apply warmth to the extremities.

6. If the abdominal pain be severe, morphine must be given.

Chronic Poisoning.—1. Remove the cause.

2. Administer tonics and advise fresh air.

3. For neuritis electrical treatment and strychnine or gelsemium internally.

Poisoning by Salvarsan.—Several cases of serious poisoning have resulted from administration of salvarsan. Shortly after an injection there may appear headache with some colic and diarrhœa ensuing, or even collapse. More severe cases show cyanosis, rapid and feeble pulse and marked dyspnœa. Cutaneous eruptions are common, and cases of renal irritation or even acute nephritis have been noted. In most cases where death has occurred, parenchymatous degeneration has been found in the kidneys and liver. Sometimes the symptoms are mental in character, ranging from mental confusion or excitement to convulsions and epileptiform attacks.

Detection of Arsenic

1. **Marsh's Method.**—The Marsh apparatus consists of a gas-generating flask containing arsenic-free zinc and hydrochloric acid; the hydrogen generated is passed through a calcium chloride drying tube, and finally through a hard glass tube which is drawn to a point to form a jet. The hydrogen is lit at the jet, and in order to test the freedom of the materials from arsenic the jet is allowed to play on a cold porcelain surface for some time; should no brown stain deposit the apparatus is free from arsenic. The suspected material is now added to the generating flask and the nascent hydrogen combines with the arsenic to form the gaseous arseniuretted hydrogen; this on being burnt in the jet deposits a brownish-black stain of arsenic on a cold surface. The stain is soluble in bleaching-powder solution which differentiates it from an antimony stain.

2. **Fleitmann's Test.**—A convenient and rapid method of detecting arsenic is to generate hydrogen in a test-tube from zinc and sodium hydrate or hydrochloric acid. In the former case slight heat is necessary, but on no account should the mixture be boiled. The arsenical material is added to the test-tube and the gas which is evolved is allowed to act on a piece of filter paper moistened with silver nitrate solution held at the mouth of the test-tube. If arsenic be present a brown to black stain of reduced silver appears.

3. **Biological Method.**—The suspected material is placed in a test tube along with some liquid culture medium. The tube is sterilised and then infected with a culture of Penicillium brevicaule. After closing the tube with a rubber stopper the tube is placed in an incubator at 30° C. Should, within three days, a garlic-like odour develop, arsenic is present. Penicillium brevicaule has the power of forming from the arsenic a gaseous substance which is probably diethylarsine.

For other tests and for the method of quantitative estimation, toxicological textbooks must be consulted.

Preparations

1. Acidum Arseniosum (B.P., U.S.P.). As_4O_6—Arsenious Oxide, Arsenious Anhydride, Arseni Trioxidum. Characters, stratified opaque masses, or white powder, soluble 1 in 100 of cold, 1 in 10 of boiling water; the watery solution is odourless, tasteless and almost neutral.
   Dose: $\frac{1}{64}-\frac{1}{16}$ gr. (1–4 mg.).
   (*a*) Liquor Arsenicalis (B.P., U.S.P.). "Fowler's Solution," a reddish alkaline solution of potassium arsenite in water containing Tinct. Lavandulæ Co.; strength 1 per cent.
   Dose: 2–8 min. (12–50 cl.).
   (*b*) Liquor Arsenici Hydrochloricus (B.P., U.S.P.). An acid watery solution of arsenious acid; strength 1 per cent.
   Dose: 2–8 min. (12–50 cl.).
   (*c*) Liquor Acidi Arseniosi (B.P.C.). Compatible with both acids and alkalis; strength 1 per cent.
   Dose: 2–8 min. (12–50 cl.).

(*d*) Mistura Ferri Arsenicalis (B.P.C.). Contains 2 min. of arsenical solution, 5 gr. of iron and ammonium citrate, and 10 min. of Tinct. Calumba in each fluid ounce.
Dose : ½–1 fl. oz. (15–30 ml.).

(*e*) Liquor Potassii Arsenatis et Bromidi (B.P.C.). Clemen's Solution. Contains 1 per cent. potassium arsenate and ½ per cent. bromine.
Dose : 2–8 min. (12–50 cl.).

(*f*) Pasta Arsenicalis (B.P.C.). Contains arsenious acid 50, morphine acetate 25, and creosote to form a stiff paste. (*Obsolete.*)

(*g*) Pilulæ Asiaticæ (B.P.C.). Each contains ½ gr. arsenious acid, ¾ gr. black pepper, and ⅙ gr. extract of gentian.
Dose : 1–2 pills daily. (Occasionally useful.)

(*h*) Pilulæ Ferri et Arsenici (B.P.C.) Each contains 3 gr. exsiccated ferrous sulphate and $\frac{1}{60}$ gr. arsenious acid.
Dose : 1–2 pills daily. (Useful method of giving iron and arsenic.)

2. Acidum Arsenicum (B.P.C.). $H_3AsO_4,\frac{1}{2}H_2O$. Characters, colourless, deliquescent crystals.
Dose : $\frac{1}{60}-\frac{1}{12}$ gr. (1–5 mg.). (Acts more slowly and is less poisonous than arsenious acid, otherwise of no advantage.)

3. Sodii Arsenas Anhydrosus (B.P., U.S.P.). Na_2HAsO_4. Characters, a white powder, soluble 1 in 6 of water with alkaline reaction; this is the exsiccated salt.
Dose : $\frac{1}{40}-\frac{1}{10}$ gr. (1·5–6 mg.).

(*a*) Liquor Sodii Arsenatis (B.P., U.S.P.). A 1 per cent. solution of anhydrous sodium arsenate in water.
Dose : 2–8 min. (12–50 cl.).

(*b*) Injectio Sodii Arsenatis et Ferri (B.P.C.). Contains 0·5 per cent. sodium arsenate and 4 per cent. iron and ammonium citrate.
Dose : Hypodermic, 5–10 min. (3–6 dl.). (*Obsolete.*)

4. Sodii Arsenas (U.S.P.). $Na_2HAsO_4,7H_2O$. Characters, colourless prismatic crystals, soluble in water.
Dose : $\frac{1}{10}$ gr. (6 mg.). Efflorescent and liable to vary in composition.)

5. Potassii Arsenas, KH_2AsO_4 (B.P.C.). Characters, white crystals soluble in water, solution acid.
Dose : $\frac{1}{20}-\frac{1}{10}$ gr. (3–6 mg.). (This salt is more stable and less liable to form incompatibility than Sodii Arsenas.)

6. Ferri Arsenas (U.S.P.). $Fe_3(AsO_4)_2,6H_2O$. Characters, greenish powder, amorphous, without taste, insoluble.
Dose : $\frac{1}{16}-\frac{1}{4}$ gr. (4–16 mg.). (Contains too little iron to be of much use in treatment.)

7. Ferri Citro-arsenis Ammoniatus (B.P.C.). Characters, green or yellowish-green deliquescent scales.
Dose : $\frac{1}{40}-\frac{1}{2}$ gr. (1·5–30 mg.). (Occasionally used as hypodermic injection.)

8. Arsenii Iodidum (B.P., U.S.P.). AsI_3. Characters, small crystals of an orange colour, soluble 1 in 11 of water, with acid reaction.
Dose : $\frac{1}{20}-\frac{1}{5}$ gr. (3–12 mg.).

(*a*) Liquor Arsenii et Hydrargyri Iodidi (B.P., U.S.P.). A clear, yellow, watery solution, taste metallic; contains 1 per cent. of arsenious and mercuric iodides.
Dose : 5–20 min. (3–12 dl.). (A useful method of giving arsenic and mercury.)

9. Arsenii Bromidum (B.P.C.). $AsBr_3$. Characters, white deliquescent crystals, decomposed by water.
Dose : $\frac{1}{60}-\frac{1}{15}$ gr. (1–4 mg.). (Of little value.)

(*a*) Liquor Auri et Arsenii Bromatus (B.P.C.).
Dose : 5–10 min. (3–6 dl.). (Occasionally used in epilepsy.)

10. Arsenii Chloridum (B.P.C.). $AsCl_3$. Characters, colourless, oily, fuming liquid, decomposed by water.
Dose : $\frac{1}{60}-\frac{1}{15}$ gr. (1–4 mg.). (*Obsolete.*)

11. Quininæ Arsenas (B.P.C.). $C_{20}H_{27}N_2O_6As,2H_2O$. Characters, white, silky needles, slightly soluble in water.
Dose : $\frac{1}{16}-\frac{1}{8}$ gr. (4–8 mg.). (Occasionally used in malaria, but contains very little quinine.)

12. Strychninæ Arsenas (B.P.C.). $C_{21}H_{25}N_2O_6As,\frac{1}{2}H_2O$. Characters, small white acicular crystals, soluble in water.
Dose : $\frac{1}{60}-\frac{1}{15}$ gr. (1–4 mg.). (For phthisis. *Obsolete.*)

13. Acidum Cacodylicum (B.P.C.). $C_2H_7AsO_2$. Characters, colourless, odourless crystals, hygroscopic.
Dose : ¼–1 gr. (16–60 mg.).

(*a*) Sodii Cacodylas (B.P.C.). $As(CH_3)_2O_2Na$. Characters, deliquescent white crystals, solution neutral.
Dose : ¼–1 gr. (16–60 mg.).

(*b*) Magnesii Cacodylas (B.P.C.).
$((CH_3)_2AsO_2)_2Mg,H_2O$. Characters, white neutral powder, soluble in water.
Dose : $\frac{1}{4}$–$\frac{3}{4}$ gr. (16–48 mg.).

(*c*) Ferri Cacodylas (B.P.C.).
$((CH_3)_2AsO_2)_3Fe$. Characters, yellow amorphous powder, soluble in water.
Dose : $\frac{3}{4}$–5 gr. (5–30 cg.) daily; hypodermically, $\frac{3}{4}$–$1\frac{1}{2}$ gr. (5–9 cg.) daily.

(*d*) Quininæ Cacodylas (B.P.C.).
$C_{22}H_{31}N_2O_4As$. Characters, acicular crystals, soluble in water.
Dose : $\frac{1}{4}$ – 1 gr. (16–60 mg.).

14. Sodii Aminarsonas (B.P.C.). $C_6H_7NO_3AsNa$, $4H_2O$; Atoxyl, Arsamin, Soamin. Characters, white crystalline, odourless powder, slightly saline taste, soluble in water.
Dose : $\frac{3}{4}$–3 gr. (5–20 cg.).

15. Sodii Metharsenis (B.P.C.).
$CH_3AsO_3Na_2,6H_2O$; Arrhenal, Arsenyl. Characters, transparent, colourless crystals, soluble in water.
Dose : $\frac{1}{2}$–2 gr. (3–12 cg.).

LITERATURE ON SALVARSAN

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ANTIMONY

Antimony is a drug closely allied in its effects to arsenic, and in a less degree to phosphorus. It approaches more than either of these to the characters of a heavy metal. Antimony salts are absorbed with difficulty and possess irritant properties, their chief uses being as diaphoretics and emetics.

Chemistry of Antimony

Antimony, Sb, 120·2, is a bright crystalline metal; it may also be obtained in amorphous form. Metallic antimony is not employed in medicine nowadays, but formerly cups made of antimony, called "Pocula emetica," were used; wine kept in them dissolved sufficient antimony to bring about an emetic action. The sulphides of antimony are of little interest medically. The chemistry of antimony resembles that of arsenic; thus, there is antimonious oxide, Sb_4O_6, and antimonic oxide, Sb_2O_5.

Organic Antimony Preparations.—Antimony does not form organic compounds with as much freedom as arsenic. Tartar emetic is potassium antimonyl-tartrate and contains the antimonyl radical, SbO. Several compounds have been prepared of an organic nature, but the subject is largely in the experimental stage and no good purpose would be served by detailing the chemistry of substances which have not yet proved of practical interest.

Pharmacology of Antimony

External.—Antimonious chloride, if applied to the skin, is an irritant escarotic or caustic, acting by combining with albumen in the same way as heavy metals. Tartar emetic is also an irritant, and if rubbed on the skin in solution or as an ointment it gives rise to erythema and a papular eruption which is distributed round the sweat and sebaceous glands; the papules at a later stage develop into pustules, and these may coalesce and form abscesses. If extensive applications are made actual necrosis and ulceration of the cutaneous tissues may result. Antimony salts are absorbed from the broken skin and mucous surfaces and pass into the general circulation. Tartar emetic, when injected subcutaneously or intravenously, gives rise to great pain, and is liable to cause ulcerative processes.

Internal.—1. *Digestive System.*—Small doses of antimony entering the stomach give rise to irritation of the stomach walls, and larger doses cause a feeling of nausea and depression resulting in actual vomiting. Accompanying the act of emesis and explicable by it are the symptoms of salivation, a feeling of coldness with perspiration and increased rapidity of the pulse

and respiration. The pharmacology of antimonial vomiting is not settled; the preponderance of evidence is in favour of a local irritant action on the stomach, but some authorities are inclined to ascribe the effects in part at least to a stimulation of the vomiting centre. The evidences for and against this latter hypothesis may be shortly stated. Majendie found that even when the stomach was excised tartar emetic gives rise to vomiting efforts; and Mosso found that section of the intra-abdominal vagus prevented the occurrence of vomiting when tartar emetic was given by the mouth, but still caused it when given intravenously: on the other hand it may be that in Majendie's experiment the vomiting efforts were induced by irritation of some other part of the intestinal tract; it has been proved that, to produce emesis by intravenous injection, much larger doses are necessary than by the mouth; and with intravenous administration the vomiting is longer delayed; further, in cases where emesis occurs the first vomit always contains some of the antimony, showing that it is excreted by the stomach. It therefore appears probable that the vomiting is due to the local irritant action of antimony upon the stomach. The emesis caused by antimony is neither certain nor rapid, and is accompanied by severe depression.

Antimony salts are not absorbed as rapidly as arsenical salts, and, should vomiting not occur, the antimony is retained in the stomach and passes into the intestine. In both situations it may cause an inflammation and direct destruction of the mucous membrane of the intestinal tract; further, after absorption the antimony salts produce a capillary paralysis, limited largely to those of the splanchnic area which results in blood stasis and exudation from intestinal capillaries with consequent excoriation of the overlying mucous membrane. Thus the action of antimony in producing a severe enteritis is of twofold origin; the diarrhœa in such cases consists of sero-albuminous fluid with portions of detached mucous membrane.

2. *Action on the Blood.*—Antimony is slowly absorbed into the blood and is taken up from it and stored in the liver. It does not appear to have any important influence on the corpuscular elements. Diminution of the red cells and increase in the leucocytes have been recorded, while the alkalinity is said to be decreased.

3. *Metabolism.*—Small doses of antimony affect metabolism in much the same way as does arsenic; they diminish metabolism, lessen the excretion of urea and increase the subcutaneous fat. Large doses have the opposite effect; oxygenation is diminished, there is an increase in the excretion of nitrogenous products, and diminution of glycogen in the liver, while fatty degeneration occurs in the internal organs. In view of the fact that antimony salts are so irritant and so slowly absorbed the use of them as metabolic stimulants is not advisable.

4. *Circulatory System.*—In animals antimony acts as a direct depressant to the heart muscle; the beat is at first slightly accelerated, but later becomes slow and weak. The blood pressure falls, due partly to weakness of the heart and partly to the action of antimony in causing dilatation of the peripheral arteries and capillaries, especially those of the splanchnic area; that the action is peripheral is proved by the fact that after antimony has been taken stimulation of the splanchnic nerves has no effect in raising blood pressure. In frogs heart-block has been noted, and the heart is arrested in diastole, the muscle being found incapable of responding to stimuli. In man there is usually at first an increase in the rate of the pulse, which becomes weak and often irregular; these effects are due to reflexes from nauseation; but if the antimony is not vomited it produces a slowing of the pulse by about ten beats per minute, and a fall in the blood pressure as in animals.

5. *Respiratory System.*—The preliminary acceleration of respiration seen after antimony is due to reflexes arising from the stomach; on absorption of the antimony respiration is slow and under poisonous doses it becomes irregular. Its action as an expectorant in liquefying the secretion is a consequence of its nauseating action.

6. *Neuro-muscular System.*—The feeling of depression and symptoms of nervous collapse are due to the gastric irritation, but antimony also has a direct depressant action on nervous tissues and muscle. The reflex centres in the spinal medulla are the first to be affected, and the sensory cells are affected before the motor.

In man nervous symptoms are rare and seldom occur short of poisoning.

7. *Skin, Mucous Membranes and Glands.*—Given internally, antimony preparations increase the perspiration, salivary secretion and bronchial secretion. The exact mechanism of this is doubtful; it must largely be ascribed to the stomach irritation which leads to reflex secretion of the various glands, but some authorities ascribe these actions to peripheral vascular dilatation. In persons who tolerate antimony sweating is not common. While definite cases of skin eruptions due to antimony are rare, they have been recorded, and it appears probable that antimony is partially excreted in the cutaneous tissues. On the skin of frogs it acts like arsenic in causing softening of the epithelial structures, with the result that they peel off readily.

8. *Temperature.*—The fall in temperature characteristic of antimony is frequently considerable and may amount to several degrees in a few hours. This antipyretic action is explainable on the following grounds: (*a*) the slowing and weakening of the heart; (*b*) the dilatation of peripheral capillaries; (*c*) profuse perspiration; (*d*) general collapse. The effect is accompanied by a feeling of cold.

9. *Action on Parasites.*—Antimonial preparations, like arsenical, have specific toxic powers towards protozoal parasites. Thus they have been shown to be toxic to spirochætes, but they appear to have no remarkable action on the progress of the disease; on the other hand, upon trypanosomes they are more active and appear to be more rapid in action than arsenical preparations. If a rat with numerous trypanosomes in its blood is treated with antimonyl sodium tartrate, the parasites disappear in half an hour. The trypanosomes are not, however, permanently destroyed, they ultimately return and acquire the power of resisting antimony. Rowntree and Abel, using triamide of antimony tri-thio-glycollic acid and sodium antimony di-thio-glycollate found that they were efficacious in the treatment of trypanosomiasis in rats, dogs and rabbits; they are of most use soon after infection has taken place. If injection is delayed beyond forty-eight hours the animal improves, but relapses occur, demanding repeated injections. Intravenous injections of antimonial sodium tartrate have also given hopeful results in animals, and one-sixth of a grain was given in man with good results; even the metal antimony in a fine state of subdivision has been employed with more or less success. Meantime these results must be considered as *sub judice* as the treatment is merely in the experimental stage.

Therapeutics of Antimony

External.—Tartar emetic was formerly used as a counter-irritant, but this is now, or should be, discontinued.

Internal.—1. *Digestive System.*—Antimonial preparations have a limited field of use for their emetic properties; they are almost useless in cases of poisoning since their action is slow and uncertain and their depressing after-effects undesirable.

2. *Respiratory System.*—The vinum antimoniale is still employed in acute bronchitis where the expectoration is difficult to remove; laryngitis is also amenable to treatment by antimony; it has been advised also in asthma and was formerly the standard remedy in acute pneumonia. The laryngitis and capillary bronchitis of children often do well under antimony. In all cases the dose should be small, frequently repeated, and its action watched for the occurrence of depression. Vinum antimoniale is the least depressant form of administering the drug.

3. *Nervous System.*—Formerly antimony was given to produce depression, collapse and relaxation of muscles previous to operations. It will quiet the excitement of patients suffering from mania and delirium tremens, but it is not the remedy which should be employed.

4. *Cutaneous System.*—Occasionally antimonial preparations are useful as diaphoretics in acute febrile conditions where they also reduce the temperature. As diaphoretics for relieving the work of the kidneys they are far inferior to pilocarpine. Antimony has been advised to replace arsenic in the treatment of certain skin diseases; its value is chiefly in acute and chronic inflammatory conditions, where 5 min. of the wine may be given in water after meals. Solutions of antimony chloride have also proved of benefit as local applications.

5. *Temperature.*—As an antipyretic the use of antimony should be confined to robust subjects and the effect of the dose carefully watched, since its action in lowering the temperature is purely of a depressant character. Its position has been completely usurped by the modern synthetical antipyretics.

6. *Sleeping Sickness.*—The use of antimonial salts as remedies for sleeping sickness cannot yet be endorsed; the treatment has not proved curative except in very early stages and in isolated cases.

Toxicology of Antimony

Acute Poisoning.—Immediately on taking a poisonous dose of antimony a metallic taste is felt in the mouth; this is followed by a feeling of malaise and a hot and burning sensation extending from the mouth to the stomach, accompanied by constriction of the throat. Vomiting sets in very rapidly, the vomit may be stained with blood, and is accompanied by acute pain in the stomach and intestines. Subsequently there is watery diarrhœa, great increase in the rapidity of the pulse and respiration, which latter is shallow and may be irregular, profuse perspiration, salivation, and it may be expectoration. Soon collapse sets in, with slowing and weakening of the pulse and respiration, fall of blood pressure, coldness of the skin and extremities, often cyanosis and giddiness, unconsciousness, and the appearance of general convulsions of a clonic nature. Finally, paralysis of the heart ends the picture. Occasionally vomiting is long delayed and symptoms of a narcotic character are observed.

Post-mortem.—The stomach is red and inflamed, portions of the superficial mucous membrane are absent, or ulcerated patches are seen, and the organ is often filled with a slimy mucus.

The mouth, œsophagus and stomach often show papules and pustules, and occasionally inflammatory changes have been seen in the lungs. The liver, kidneys and other organs may show traces of fatty degeneration.

Fatal Dose.—3–6 dg. (5–10 gr.) of tartar emetic.

Fatal Period.—Varies from a few hours to several days.

Chronic Poisoning.—The earliest symptoms are usually catarrhal inflammations and stomatitis, but these may not be observed, and the first recognised symptoms are frequent attacks of vomiting and diarrhœa with persistent thirst and excessive depression. Cramps in the limbs are common and may be severe. The pulse is weak and the skin cold and covered with a clammy perspiration. The liver is enlarged from fatty degeneration.

Treatment of Poisoning. *Acute.*—1. Wash out the stomach thoroughly, preferably with a solution of tannic acid. Emetics are not necessary, but in cases of acute poisoning where vomiting has not occurred it is advisable to wash out the stomach at once. If tannic acid is not available, wash out with boiled tea.

2. Administer magnesia, albumen and milk in large doses.

3. Administer stimulants and warmth to the surface as early as possible to avoid collapse.

4. For abdominal pains and cramps in the limbs administer morphine.

Detection of Poison. (For details see under *Arsenic.*) 1. *Marsh's Test.*—Antimony salts subjected to Marsh's test give a black stain on the porcelain which is insoluble in bleaching powder, but which dissolves in dilute hydrochloric acid. On passing sulphuretted hydrogen into such a solution the orange sulphide of antimony is obtained as a precipitate, whereas arsenic yields a yellow precipitate. Again, on heating the delivery tube behind the jet antimony deposits as a black ring near the flame, but arsenic only at some distance from the flame.

2. *Fleitmann's Test.*—Antimony does not respond to this reaction.

3. *Biological Test.*—Antimony salts fail to produce the odour of garlic.

Preparations

1. Antimonium Nigrum Purificatum (B.P.C.). Sb_2S_3. Character, greyish black crystalline powder (used to prepare the sulphide).

2. Antimonium Sulphuratum (B.P.). Characters, dull red powder, without odour or taste.
   Dose: 1–2 gr. (6–12 cg.).

3. Antimonii Oxidum (B.P.). Sb_2O_3. Characters, greyish white powder, insoluble in water.
   Dose: 1–2 gr. (6–12 cg.).
   (*a*) Pulvis Antimonialis (B.P.). "James's powder." Contains 1 of antimonious oxide in 2 of calcium phosphate.
   Dose: 3–6 gr. (2–4 dg.).

4. Antimonium Tartaratum (B.P., U.S.P.). $(K(SbO)C_4H_4O_6)_2H_2O$. Characters, colourless transparent crystals, taste sweet and metallic, soluble in water.
   Dose: diaphoretic, $\frac{1}{25}$ – $\frac{1}{8}$ gr. (2·5–8 mg.); emetic, $\frac{1}{2}$ – 1 gr. (3–6 cg.).
   (*a*) Vinum Antimoniale (B.P., U.S.P.).
   Dose: 10–30 min. (6–18 dl.); emetic, 2–4 fl. (dr. 8–16 ml.). (Less depressant than tartar emetic and preferable to it.)
   (*b*) Unguentum Antimonii Tartarati (B.P.C.). (*Obsolete.*)

5. Antimonii Chloridum (B.P.C.). $SbCl_3$. Characters, colourless deliquescent crystals. (*Obsolete.*)
   (*a*) Liquor Antimonii Chloridi (B.P.C.). (*Obsolete.*)

W. J D.

ALCOHOL

Alcohol is usually held to mean ethyl alcohol, C_2H_5OH, the second of the series of primary fatty alcohols, whose general formula is $C_nH_{2n+1}OH$. It is formed by distillation from solutions which have undergone fermentation by yeast, the yeast acting on sugars which may be primarily present, or which may be first produced from starchy material by the action of enzymes. Thus beer is prepared by the fermentation of malt with yeast, and the further addition of hops or some other bitter. There are, however, many modified methods of making beer, and often glucose from other sources is itself directly fermented. Wines are produced by the fermentation of grape and other fruit juices. Originally, Scotch whisky was prepared by the distillation of fermented barley malt, but nowadays other sources of alcohol are used, such as maize and molasses and even sawdust. Brandy is formed by the distillation of wine and contains more volatile ethers than other spirits, for these latter are formed in wine as it matures. Gin is first prepared as whisky and then redistilled with flavouring agents such as juniper berries and coriander seeds.

The following table shows the percentage

amount of alcohol in the best-known alcoholic beverages—

Beer, 4–5 per cent.
Cider, 5–10 per cent.
Hock, claret, 8–11 per cent.
Port, 16–18 per cent.
Marsala, 14–24 per cent.
Orange wine, raspberry wine, 10–12 per cent.
Champagne, 8–11 per cent.
Sherry, Madeira, 13–18 per cent.
Gin, 31 per cent.
Rum, liqueurs, 40–50 per cent.
Whisky, 44–50 p. c.
Brandy, 48–56 p. c.
Rectified spirit, 84 per cent. (by weight).
Methylated spirit, 90 per cent. (by volume).

In the fermentation of the sugars, other homologous alcohols of the fatty series, such as propyl, butyl, amyl, hexyl, heptyl and octyl alcohols are formed in addition to ethyl alcohol, and also various aldehydes and ethers, acetic and succinic acids. Only a small proportion of the sugars (about 5 per cent.) are converted along these collateral tracks. Some of these by-products of alcoholic fermentation, such as amyl alcohol, butyl and propyl alcohols and the fatty acids are called fusel oil, but they diminish or disappear with age, or can be removed by distillation with charcoal. The composition of fusel oil varies considerably with the source from which the alcohol is obtained, amyl alcohol being abundant in potato fermentation, and butyl alcohol in beetroot fermentation.

Alcohol is a transparent, colourless, volatile liquid with an agreeable odour and burning taste. Spiritus Rectificatus (B.P.) contains 90 per cent. by volume and 85·68 per cent. by weight of alcohol and 14·32 per cent. by weight of water. Specific gravity 0·8337. Alcohol absolutum (B.P.) contains 99·4 per cent. by volume of ethyl alcohol and has the specific gravity 0·795. Alcohol Dilutum (U.S.P.) is prepared by mixing equal volumes of alcohol (94·9 per cent.) and distilled water.

Alcohol is miscible in all proportions with water, ether and chloroform. Proof spirit (sp. gr. 0·920) contains 49·24 of ethyl alcohol, and spirits are described as so many degrees over or under proof, according to the quantity of distilled water which must be added to, or deducted from, 100 volumes in order to produce proof-spirit strength. Ninety per cent. alcohol corresponds to nearly 58 over proof, so that 100 volumes of this solution contains as much alcohol as 158 volumes of proof spirit. Methylated spirit is a mixture of nineteen parts of alcohol of a strength of not less than 50 over proof (about 86 per cent. alcohol) and one part of commercial wood naphtha.

The Pharmacological Action of Alcohol

External Action of Alcohol.—The external application of alcohol to the skin differs according as to whether it is allowed to evaporate or not. If allowed to evaporate, it absorbs heat from the tissues and in so doing produces a marked local cooling effect. Repeated application in this way brings out another effect, namely, a hardening of the skin. This hardening is due to the coagulating action of alcohol on protoplasmic and protein substances. The coagulation of proteins by alcohol is a well-known action and is particularly interesting because for each protein substance there is usually a temperature below which alcohol only precipitates the protein, while above the specific temperature true coagulation takes place. For instance, serum albumen, if kept cold, is precipitated by 50 per cent. alcohol and redissolves on diluting with water; while above 16° C. the same percentage of alcohol will cause a true coagulation, a change which is not reversible. The body temperature is above this critical point, so that only the coagulating action of alcohol on proteins is of therapeutic interest.

When alcohol is continuously applied to the skin, and evaporation prevented, it begins to show irritant properties. The blood-vessels now become dilated and local redness is produced. This is in contradistinction to the blanching and vaso-constrictor effect evident when alcohol is allowed to evaporate from the skin. The vaso-dilator effect, after a more prolonged action, may go on to inflammation.

The antiseptic action of alcohol is also of interest, for, by killing bacteria present in wounds or on the skin, it prevents putrefactive changes. However, compared to such a substance as chloroform, the antiseptic action of alcohol is small.

Gastro-intestinal Tract, *Action of Alcohol on the Mucous Membrane.*—This action of alcohol is similar to that described above in the case of the skin. Since, however, mucous membrane cells have no such protective layer as the stratum corneum, they are much more susceptible to the action of alcohol. Alcohol stimulates the epithelial cells of the mouth and stomach in comparatively small doses and, in larger doses, acts as an irritant. Thus small percentages of alcohol produce a vaso-dilatation of the blood-vessels underlying the mucous membrane, which is of temporary duration and, no doubt, to some extent, is partially responsible for the feeling of well-being and internal warmth which follows the imbibing of alcoholic beverages. The stimulating action of alcohol will also increase the amount of those digestive juices which are normally called forth reflexly by stimulation of the mucous membrane. For instance, the salivary secretion and the secretion of the gastric glands are increased. When any irritant substance is applied to the alimen-

tary mucous membrane, its cells try to protect themselves by secreting an impermeable layer of mucus. This reaction is seen in the case of alcohol, while, in addition, large percentages of alcohol produce the protein-coagulating effect seen in the case of the skin. For instance, if brandy be retained in the mouth for some time the mucous membrane assumes a white and corrugated appearance, due to the dehydration of the cells and the partial coagulation of the proteins in the protoplasm. In such a case also there would be an undoubted diminution in the sense of taste in consequence of the partial paralysis of the taste nerve-endings by the alcohol. The action of large quantities of alcohol on the mucous membrane of the stomach is well described by Beaumont (1) in his observation on Alexis St. Martin. He writes as follows—

"St. Martin has been drinking ardent spirits pretty freely for eight or ten days past: complains of no pain, nor shows symptoms of any general disposition: says he feels well and has a good appetite.

"*August* 1. 8 *a.m.*—Examined stomach before eating anything: inner membrane morbid: considerable erythema, and some aphthous patches on the exposed surface.

"*August* 3. 7 *a.m.*—Inner membrane of stomach unusually morbid: the erythematous appearance more extensive, and spots more livid than usual: from the surface of some of which exuded small drops of grumous blood, the aphthous patches larger and more numerous, the mucous covering thicker than common. . . . The gastric fluids . . . were viscid with a large proportion of thick ropy mucus and considerable muco-purulent matter slightly tinged with blood."

The interesting point about this morbid condition is that St. Martin felt little or no discomfort at the time.

It is clear, then, that the effect of alcohol on the alimentary mucous membrane is different according as whether the percentage strength is small or large. In the first case, a stimulant action is evident, with its corresponding physiological results, whereas high percentages of alcohol produce toxic results with large mucous secretion, local erythema, and partial coagulation of the cell elements. Whether continued drinking of small percentages of alcohol, as are present in beer, would ultimately produce the morbid condition produced quickly by spirits, and whether such a result is entirely due to the alcohol present, there is no evidence, but the rapid rate of absorption of diluted alcohol from the intestine seems to be contrary to such a supposition.

Action of Alcohol on the Secretion and Activity of Digestive Ferments.—By stimulating the mucous membrane of the mouth, alcohol reflexly causes an increased flow of saliva and therefore may be considered an adjuvant to carbohydrate digestion. It must be remembered, however, that any such increased secretion may be more than counterbalanced if the volume of fluid be so great as to bring about a large dilution of ferment and foodstuff, and this more especially, since Pawlow showed that water in itself has an inhibitory action on salivary secretion.

Since the end products of salivary digestion have the power of liberating gastric secretion from the pyloric end of the stomach into the blood stream, it follows that, if alcohol stimulates carbohydrate digestion, it also stimulates the secretion of gastric juice. But, in addition to this indirect effect, alcohol is a direct stimulant of gastric juice. Chittenden and Mendel (2), confirming the increased secretion of gastric juice observed by other workers, further noted that apart from the direct action when in contact with the mucous membrane of the stomach, alcohol present in the blood stream after absorption causes an increased and lasting flow of gastric juice containing more solids and acid than normally. The increased flow produced by alcohol placed in the stomach they ascribed to an irritating action on the nerve-endings, but it seems more probable, in view of Pawlow's experiments demonstrating the inefficiency of mechanical irritants in the stomach, that the increased secretion depends on a chemical action of the alcohol similar to the secretion caused by meat extracts. High percentages of alcoholic solutions, on the other hand, especially if taken continuously, bring about pathological changes which antagonise any beneficial effect previously produced by the alcohol, and, as in the observations of Beaumont quoted above, the gastric juice becomes "mixed with thick ropy mucus and muco-purulent matter, tinged with blood and resembling the discharge from the bowels in some cases of chronic dysentery." Further, Pawlow found that absolute alcohol introduced into the stomach for a few minutes had a similar action on the gastric secretion to that of irritants like a 0·2 per cent. solution of mercuric chloride, a 10 per cent. solution of silver nitrate and a strong solution of oil of mustard. In each case a more or less copious secretion followed, containing an enormous amount of mucus, and sometimes only mucus instead of juice was secreted.

But a further question arises. Granted that alcohol is a stimulant to salivary and gastric secretions, how does its presence affect the digestive action of these ferments? Since alcohol has antiseptic properties, it might be expected that it would have an inhibitory

action on ferments. So it has, but this inhibitory action is not evident till the stomach contains from 5 to 10 per cent. of alcohol. Below 5 per cent. the effect of the alcohol is not inhibitory. On the other hand, above 20 per cent. of alcohol the action of pepsin is completely arrested, although even in the presence of 45 per cent. alcohol the action of ptyalin on starch proceeds to some extent. While it is true that alcohol itself has but little action on salivary digestion, it is important to remember that alcoholic beverages, particularly rum, sherry and claret, practically inhibit the digestion of carbohydrate in the smallest doses. Their inhibitory action depends on other constituents than alcohol—in the case of wines the acid they contain. Trypsin is more susceptible to the influence of alcohol than pepsin, and in the presence of only 2 or 3 per cent. of alcohol its action is retarded. Even when ferment action is considerably retarded by alcohol, it begins again on dilution or with the disappearance of the alcohol. Now alcohol is rapidly absorbed from the intestine into the blood stream and even in the stomach. For instance, Mendel and Chittenden and Jackson found that if 50 c.c. of a 20 per cent. solution of alcohol be placed in the stomach of a dog with the pyloric orifice tied, it had all disappeared from the stomach at the end of half an hour. Consequently, the retarding effect of alcohol on the action of digestive juices is not an important factor, for, besides being absent when less than 5 per cent. alcohol is present, the rapid removal of alcohol from the digestive tract causes any inhibitory action to be only of a temporary nature.

The Effect of Alcohol on Gastro-intestinal Movement.—Alcohol also influences the stomach movements in addition to its action on ferment secretion. Under the influence of small quantities of alcohol the stomach movements are increased, so that, with increased peristalsis, food is more rapidly propelled into the duodenum during digestion. For instance, it has been shown that olive oil, which has a marked inhibitory action on stomach movements, is more quickly forced into the duodenum when alcohol is present. The increased propulsion in this case may, of course, be due to the solvent action of the alcohol on olive oil, tending thereby to reduce the inhibitory action of the latter. Whether this is the explanation or not, alcohol is undoubtedly a useful aid to fat digestion in consequence of this solvent action.

Besides being itself rapidly absorbed from the stomach and intestine, alcohol appears to have the power of aiding the absorption of other substances. Thus, it is said that chloral injected into the stomach of a dog with pylorus occluded does not produce its soporific effect, but, if a little alcohol be added, narcosis results.

To sum up, alcohol in small doses increases the flow of digestive juices, has an inhibitory action on ferments of a temporary nature when above 5 per cent., increases peristalsis, aids the digestion of fats by dissolving them and assists the absorption of some substances. On the other hand, the action of alcohol as found in spirits is toxic, diminishing the secretion of digestive juices, causing a large secretion of mucus with erythema, and ultimately destroying the mucous membrane and also inhibiting ferment action.

Action of Alcohol on the Nervous System.—The action of alcohol on the nervous system is more apparent than in the case of any other system, and it is usual to associate the susceptibility of the nervous system to alcohol with the high percentage of lipoid substances present in nervous tissue. For, although alcohol does not come into the group of hypnotic drugs and so fall under the law of Overton and Meyer as to the action of this series of drugs, it is probable that it attains access to cells in consequence of its power of dissolving these lipoid substances. It is a general physiological law that the more highly organised and specialised a cell is the more susceptible is it to toxic reagents. Consequently, the cells of the cortex cerebri and of the higher nervous centres are the first to give evidence of alcoholic influence. With increasing quantities of alcohol, and increased time of action, all parts of the nervous system become involved. In the normal person, small quantities of alcohol have a noticeable effect on those activities depending upon the higher brain centres, but these effects vary greatly with the natural disposition of the person. The talkative become more verbose; the naturally silent become morose; as a rule there is a subjective feeling of light-heartedness and worries recede to the background; conversation is often brighter and may be brilliant. These results of small quantities of alcohol were once considered to be due to a stimulating action on the cortical nerve cells. Since, however, it has become clear that the function of the cortex is one of general inhibition on the lower centres of the central nervous system, it is becoming more generally believed that, from the first, the action of alcohol on nerve cells is one of paralysis, so that what appears to be the result of a stimulating action may be only a partial paralysis of a normal inhibitory mechanism. That the cortical cells are inhibitory is definitely seen in thalamic lesions when the cortico-thalamic fibres are destroyed. In such a case the emotions appear to be uncontrolled by the cortex and emotional outbursts are characteristic of the condition. The in-

hibiting action of the cortex on the para-cerebellar nuclei is also evident in decerebrate rigidity, while, finally, lesions of the pyramidal tract, resulting in the spastic condition of voluntary muscle, demonstrate the normal inhibitory influence of the cortex on the anterior horn cells of the spinal cord. It is clear, therefore, that a paralysis of the cortical cells, removing a normal, controlling, inhibitory influence, might account for the earliest symptoms of alcohol, some of which, at first sight, would be put down to a stimulating action.

Another primary function of the cerebral cortex is that of providing the animal with a sense of judgment. Sensations which reach the thalamus are "effective," whereas, when they reach the cortex, they become "discriminative." It might be expected, therefore, that anything paralysing the higher centres would result in a diminution or loss of judgment. And this is the case with alcohol. Under its influence all stages of effect are seen from the loss of self-criticism, which probably accounts for the ordinary man occasionally becoming brilliant in conversation, or the naturally modest becoming daring, to the man filled with grandiose ideas, commonly seen in such a condition as general paralysis of the insane.

A brief analysis of some of the effects of alcohol on the nervous system will now be given.

The Effect of Alcohol on the Motor Mechanism.—It is undoubtedly the case that the first action of small quantities of alcohol on the motor mechanism is to shorten the latent period for reflex actions. Kraepelin (3) found that after a small quantity of alcohol ($\frac{1}{4}-\frac{1}{2}$ fl. oz.) had been drunk, the reaction time, as tested by the time of response to a signal, was somewhat shortened in the first few minutes. Also in simple automatic action where much thought was not required, as in reading aloud, an accelerator effect was first produced by alcohol. It is this experimental evidence of the shortening of reaction time that is advanced in favour of alcohol having a stimulating action on the cells of the central nervous system. The opposite explanation advocated by Schmiedeberg and others is that, by depressing the higher cerebral centres alone, reflex action of the type studied may be quickened and that the stimulating action of alcohol is an unnecessary supposition and contrary to its other known action on the nervous system. It is necessary to add that, even in the reaction-time experiments, there is generally a depressant action of alcohol evident, following the preliminary acceleration, and that this depressant action may continue for some hours, according to the amount of alcohol imbibed.

Having noticed the effect of alcohol on simple reaction time the question now arises, what is its effect on muscular movement requiring delicate co-ordination of nerve centres? It is a matter of everyday experience that large quantities of alcohol have a most disturbing effect on all muscular co-ordination, particularly that believed to be controlled by the cerebellum. One has but to recall the loss of balance and the staggering gait of the alcoholic. But there is also evidence that small quantities of alcohol have a depressing influence on neuro-muscular co-ordination. Rifle-shooting, which is a process requiring delicate interaction between the optic nerves and those of the limbs, affords a good test for alcohol influence. Swedish soldiers were required to shoot at a target at 200 yards, slow- and quick-firing, with and without alcohol, of which about $1\frac{1}{2}$ fl. oz. (45 ml.) of brandy were given. In the slow-firing tests 30 per cent. fewer hits were made after alcohol, and in quick-firing 50 per cent. fewer. It is clear, therefore, that even small doses of alcohol impair delicate neuro-muscular co-ordination.

Another point worthy of consideration is the effect of alcohol on neuro-muscular effort, which does not involve much cerebral activity. Experiments were made by Hodge to test the comparative ability of dogs as to strength, endurance and resistance to fatigue, with and without alcohol. Dogs were made to retrieve a ball when thrown, and records were kept of the dogs who started for the ball and those that retrieved it. Out of a series of 1,400 throws, the non-alcoholic dogs retrieved 922 and the alcoholics 478. It was further noticed that the normal dogs made more attempts to retrieve than the alcoholic dogs, and were more alert, stronger and energetic. Many experiments have been made on men to test the effect of alcohol on ability to work, fatigue and endurance. In the case of ergograph experiments, when the ability of a person to lift a weight with a finger is tested, it is usual to find that the power to work is increased for the first quarter of an hour after taking alcohol, but that this power then slowly diminishes, so that, on the whole, the total amount of work done is less. Rivers and Webber (4), however, found that small doses of alcohol, 1 to 5 fl. dr. (5 to 20 ml.), had no effect on the work performed, as measured by the ergograph, when the subjects experimented upon did not know they were drinking alcohol. Other results have been recorded in comparing alcoholic (workmen with beer at their disposal) and normal gangs of soldiers doing similar work. For the first two hours the alcoholic gang worked better, but by the end of day the non-alcoholic had carried out more work. Similar results have been obtained with marching

soldiers. In all these cases of the effect of alcohol on muscular work, the tissue affected by the alcohol is undoubtedly the nervous system, and the muscles are only indirectly influenced through the nerves. It will be seen in another section that alcohol is a useful foodstuff, capable of supplying energy to the muscles; and were this the only aspect of the case, no such depressing effect as is recorded in the above experiments would be evident. An instance where the available energy value of alcohol becomes an important factor in muscular work is in the case of starving animals. In this case the added energy of the alcohol allows more work to be performed.

To sum up, then, small quantities of alcohol shorten the time of reflex action at first and also increase the ability to work for a short time, but in both cases there is a marked reaction, with a lengthening of reaction time and a diminished endurance in the respective cases.

The Effect of Alcohol on Higher Cerebral Centres.—Although, in the case of purely mechanical or automatic movement, alcohol has an accelerator influence, when conscious effort is introduced into the tests, an inhibitory influence is generally evident from the first. In other words, quality of work is usually not so good although the quantity performed may be greater. An exception to this is seen when the person tested is asked for words rhyming with a given word, in which case an improvement is seen. Experiments on the rate of adding up figures, with and without alcohol, showed that after alcohol the work done was always slower and of inferior quality. Other interesting experiments were carried out by Aschaffenburg on compositors, whose work requires not only much skilled muscular movement but also cerebral assistance, and the depressing influence of alcohol on the rate of setting up type was most clearly demonstrated. In these latter experiments it is interesting to note that the compositors themselves felt they were doing better work on the alcohol days, although this was not the case—an illustration of the effect of alcohol on judgment.

As regards memory, alcohol has a depressing influence from the first. It was shown by Kraepelin that whereas a hundred figures could be remembered after forty repetitions in a normal condition, after drinking small quantities of alcohol, only sixty figures could be remembered after sixty repetitions.

The effect of alcohol on "attention" was well demonstrated by Macdougall (5) in some experiments in which he measured the average error in marking dots rapidly passing over a slit. He compared the percentage error: (1) in a normal person; (2) after drinking 1 to 3 fl. oz. of alcohol; (3) after drinking one or two breakfast cupfuls of tea. The following is a table of his results—

TABLE OF ERRORS

	Normal.	*Alcohol.*	*Tea.*
First Series .	379	583	273
Second „ .	298	351	291

The effect of drinking 3 fl. oz. (90 ml.) of alcohol was to increase the percentage errors 53 per cent. over the normal. The marked improvement following the tea drinking is interesting. It seems clear that the effect of alcohol on attention is depressant.

The early effects of alcohol on judgment do not appear to be consistent. In such a case as merely judging perceptions, as when small differences of weight are to be determined, small quantities of alcohol seem to have an improving effect. On the other hand, it has been shown that there is a greater error in judging distances after drinking alcohol than normally. It is beyond any doubt that judgment as a rule is detrimentally affected by alcohol. For instance, the above-mentioned compositors always thought they were working better on the alcohol days, similarly the Swedish soldiers thought they were shooting more rapidly after alcohol, and Macdougall was surprised at the recorded results of his "attention" experiments.

The question of alcoholic influence on cerebration is too big for further discussion, but psychologists apparently believe all the higher psychological processes of ideation, reasoning and intellectual judgment are depressed from the first by alcohol.

Action of Alcohol on the Circulatory System.—In therapeutic doses, alcohol is a circulatory stimulant, and produces, as a general rule, slight quickening of the heart-beat, an increased force of heart-beat and a small rise of blood pressure.

The action of alcohol on the heart can be best demonstrated by experiments on the isolated heart, perfused through the coronary vessels. If small quantities of alcohol (0·01 to 0·1 per cent.) be added to the perfusion fluid, a slight stimulating action is evident and the force of the beat is increased. A similar result can be observed on the isolated ventricle. There has been considerable discussion as to the effect of alcohol on the heart-beat and its mode of action when given to the intact animal. If given by mouth it is clear that several extraneous factors might interfere with a definite result. For instance, the alcohol might produce a state of cerebral excitement, and this alone would bring about a more rapid heart-beat and a raised blood pressure. Again, a quickening of the heart-beat might be reflexly produced by the stimulating of the alcohol in

the mucous membrane of the stomach. These two factors can be eliminated by working on a pithed animal and injecting the diluted alcohol into the blood stream. If this be done and no anæsthetic such as chloroform be given, the heart-beat will be observed to give a better output, when examined by the cardiometer, as the result of alcohol administration. Diluted alcohol given by mouth in small quantities also quickens the heart-beat slightly and increases its force. If, however, large quantities of alcohol are absorbed and reach the blood stream then the heart beats more slowly. This latter action is partially due to the stimulation of the cardio-inhibitory centre in the medulla, and is not so easily produced if the vagi are previously cut.

Alcohol in therapeutic doses raises the blood pressure. This action can be demonstrated on the pithed animal with its cerebral hemispheres destroyed if no other anæsthetic such as chloroform has been previously given. The rise of blood pressure is small compared to that produced by other drugs used as cardiac stimulants. Two factors are concerned in the rise of blood pressure. The first is the increased output of the heart produced by alcohol. The second is a constriction of the blood-vessels. It is well known that alcohol produces a dilatation of the skin vessels with a concomitant feeling of warmth. It is interesting, therefore, to note that the internal and the cutaneous vessels are differently affected by alcohol. The constriction of the internal vessels can be proved by perfusing the vessels of the splanchnic area and detecting changes in volume by an oncometer. The action is probably, however, not entirely a peripheral one, but seems also to depend on a stimulating action of the alcohol on the vaso-constrictor centre in the medulla. Large quantities of alcohol produce a fall of blood pressure, diminishing the output from the heart and dilating all the blood-vessels of the body.

It is clear that alcohol in moderate doses can be regarded as a circulatory stimulant although its effectiveness is small compared to other well-known cardiac drugs.

The Influence of Alcohol on Temperature.—Alcohol has an antipyretic action, and moderate doses 1–3 fl. oz. (30–90 ml.) lower the temperature about 0·5° C. This action is due to the increased loss of heat brought about by the dilatation of the cutaneous blood-vessels. More blood is brought in contact with the atmospheric temperature and a larger heat radiation results. The blood also flows more quickly through the dilated vessels, and since the loss of heat is greater when the velocity of the moving hot body is increased (other conditions being equal), this also causes an increased loss of heat. It is evident, therefore, that the feeling of warmth, both internal and external, produced by alcohol is a delusion. The internal warmth is produced by local gastric vaso-dilatation due to the direct stimulating of the alcohol and the external warmth is due to vaso-dilatation of the skin vessels. Alcohol, therefore, is contra-indicated in conditions of stress when other food is not attainable, for it lowers the body temperature by stimulating heat loss, which is most undesirable. It has another baneful influence in such a condition, for it tends to lessen muscular activity, and by acting on the central nervous system produces lethargy and sleepiness. Since a large part of the total heat production depends on muscular movement anything which tends to lessen muscular activity will produce a lowering of temperature. These two actions of alcohol, increased loss of heat following cutaneous vaso-dilatations and diminished production due to muscular lethargy, explain the frequency of death by exposure of the alcoholic.

Effect of Alcohol on Respiration.—Alcohol has a stimulating action on respiration, but the manner in which the stimulating effect is brought about is not agreed upon. Some think it due to a direct stimulating action on the respiratory centre in the medulla. Others ascribe it to a reflex action produced by the stimulation of the gastric mucous membrane by alcohol, and similar, therefore, to that which follows the administration of an aqueous extract of mustard. Small doses of alcohol increase the oxygen absorption by about 3·5 per cent. and the carbon dioxide by 4·5 per cent. Another explanation of this stimulating action on respiration is that it is an indirect one. According to this idea, alcohol causes a fall in body temperature as the result of cutaneous vaso-dilatation, and the muscles and other organs react to this fall by an increased combustion, in an endeavour to maintain the body temperature. The increased quantity of carbon dioxide produced would then, according to this view, be responsible for the further stimulation of the respiratory centre.

It does not seem possible to decide what is the real nature of the action, and it may be due to some simple cause as the alteration of the carbon dioxide tension in the blood by alcohol or to the lowering of the threshold value of the respiratory centre to carbon dioxide tension.

Effect of Alcohol on the Kidneys.—Alcohol has a diuretic action apart from the fluid with which it is admixed. It is said to increase particularly the water element of the urine and therefore to have a stimulating action on the glomeruli of the kidneys. Some part of the diuresis produced by alcohol might, no doubt, be

explained by the increased blood pressure following its administration, causing thereby an increased flow of blood through the kidney.

In the case of whisky, and Hollands or gin, there is a further diuretic effect due to ingredients other than alcohol.

Toxicology

The foregoing account of the pharmacological action of alcohol would point to the production of various morbid conditions which might follow alcoholic excess. In the case of the alimentary canal, gastritis is commonly produced and, in addition, dilatation of the stomach is found. Another condition often found in alcoholics is cirrhosis of the liver and a large fatty liver. There is great doubt whether alcohol is the direct cause of cirrhotic liver, for it is not a uniformly produced condition, and, whereas beer- and spirit-drinkers in one country may largely escape, in other countries it is common. Some authorities ascribe it only indirectly to alcohol drinking, in consequence of bacterial action proceeding in the alimentary canal when the gastric juice secretion is suppressed by alcohol. Lately it has been suggested as being due to excessive formation and absorption of lactic acid, a product of bacterial action on sugars, into the portal circulation.

Renal disease, and particularly chronic Bright's disease, is often found associated with alcoholism, and a fatty degeneration of the kidneys may be produced.

Fatty degeneration and dilatation of the heart is sometimes produced by alcohol.

Just as the nervous system is very susceptible to physiological doses of alcohol, so also does it assume, at an early stage, a morbid condition. Such nervous conditions as delirium tremens, alcoholic insanity and peripheral neuritis are common. In the case of alcoholic insanity all stages are seen from the addiction to lying and loss of moral control to the raving maniac.

In addition to these morbid conditions, alcohol has a marked tendency to lower the general resistance of the body to infections and acute illnesses. A particular instance of this is the frequency with which pneumonia kills those addicted to the drug. A further point of interest is that toxic symptoms are by no means confined to those who take alcohol in such quantities as to make them intoxicated on occasion. Peripheral neuritis is often the first evidence of a person being an alcoholic.

Therapeutics

The chief therapeutic uses of alcohol are—

1. As an external application to the skin.
2. In shock.
3. As a digestive stimulant.
4. As a cardio-vascular stimulant.
5. To aid sleep.

As an external application, alcohol is sometimes used to harden the skin as a protection against bed-sores, and also the nipples before suckling a child. It may also be used as a lotion for alleviating inflammation, and its cooling influence is of value in cases of headache, when it is often applied in the form of eau-de-Cologne.

In shock, alcohol plays a useful part in improving the circulation and so tending to make the distribution of blood more normal by increasing the amount of blood on the arterial side at the expense of the venous accumulation. Alcohol may be given, in cases of shock, either by mouth or in the form of an enema; or, if intravenous injection of saline be carried out, a little brandy may be added to the perfusion fluid.

As an aid to digestion, alcoholic beverages may be useful during convalescence following illness and in old, debilitated people, where it will often be found to increase the appetite and the secretion of the digestive juices. It is given for such purposes well diluted with water and with the food.

As a cardiac stimulant, alcohol is useful in acute febrile disorders such as typhoid fever and pneumonia. With the object of maintaining the heart's action, alcohol 2–3 fl. oz. (60–90 ml.) per diem is sometimes prescribed from the beginning of the disease. More usually, however, it is only prescribed in such cases when the marked compressibility of the pulse and the frequency of the heart-beat suggest the onset of heart failure.

It is in acute febrile conditions, also, that the value of alcohol for inducing sleep is best seen. As is well known, sleeplessness is one of the most distressing features of typhoid fever and pneumonia, and frequently develops into delirium. The production of sleep by alcohol in these conditions is most valuable for restoring the nervous system. Alcohol diluted with hot water is also taken by old people at bedtime for producing sleep.

Another beneficial action of alcohol in acute febrile disturbances, particularly where but little nourishment can be taken, as in typhoid fever, is its value as a foodstuff, having a large amount of energy which the body can make use of without preliminary digestion.

The use of alcohol as a therapeutic agent has greatly diminished in recent years, partly because of an increased knowledge of drugs which are capable of carrying out specific actions better than alcohol, and partly because of the general recognition of the fact that the alcohol habit may be started by its therapeutic administration.

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E. M.

THE ACTIONS OF ÆTHER AND ITS ALLIES OTHER THAN THEIR ANÆSTHETIC ACTIONS

Æther

Pharmacology. *External.*—Æther is a solvent for fats and waxes, and dissolves, therefore, the sebaceous secretions of the skin and cerumen. When applied to the surface of the skin its rapid evaporation produces a refrigerant action. If the æther be directed on the epidermis in the form of a spray, the cooling of the superficial layers of the skin may be so great that actual freezing of the tissue occurs and the part becomes blanched and hard. At the same time the sensory nerve endings are completely paralysed and circulation ceases. If the part be kept frozen for some time, the loss of circulation will lead naturally to gangrene. During the process of freezing, and especially when thawing takes place, pain is commonly experienced; this is the more marked, the more rapid the freezing and thawing, hence æther, with which freezing and thawing are, on account of its higher boiling point, slower, causes less pain than substances with lower boiling points, *e. g.* ethyl chloride. Besides its local action in freezing the tissues, æther has considerable powers of penetration, and irritates the tissues, nerve endings, and vessels with which it comes in contact. The sensory nerves especially are stimulated, and by preventing evaporation of the æther, by means of a watch-glass over the area of application, a definite rubefacient effect is produced. The irritation caused by æther is, however, short in duration and is rapidly superseded by a diminution in sensibility.

Internal.—Æther may be employed as a local anæsthetic for mucous membranes, but as the tissues are much more vascular, the penetration of cold is restricted, and this applies in greater degree when inflammation has brought about dilatation of the vessels and increased blood-flow in the tissue.

In the mouth æther has a burning and objectionable taste, and, as on the skin, it causes an irritation of the mucous membrane and reflexly excites salivation, principally due to the submaxillary gland. The irritation of the mucous membrane of the mouth and nose produced by æther is directly comparable with that of the pungent volatile oils, and, as with them, the local stimulation leads to reflex excitation of the respiratory and vaso-motor centres, with the result that respiration and the pulse are increased in rapidity.

In the stomach the æthereal preparations produce a mild stimulation of the stomach wall, irritating the nerve endings, increasing muscular movements, dilating the blood-vessels and increasing the gastric secretions. Thus æther and its preparations, especially the Spiritus Ætheris and Spiritus Ætheris Compositus, are efficient carminatives; and, again by reflex action, the stomach irritation leads to a stimulation of the nervous centres, so that æther must be classed as a reflex nervous stimulant and antispasmodic. When administered in medicinal dosage by mouth, the æthereal preparations, being highly diffusible, are absorbed rapidly from the stomach and intestine; their action is therefore of an evanescent character, and, as their excretion follows rapidly, their concentration in the blood at any one time is insufficient to produce any marked specific effects on the circulatory or respiratory systems. If æther be taken internally in large amount, 4–8 fl. dr. (16–32 ml.), symptoms of intoxication, similar to those of alcohol, arise, but they are short in duration. Æther being more quickly absorbed, the excitement stage is often absent; but not uncommonly, as in alcohol, the person suffers from inco-ordination along with motor excitement, and this condition is followed by that of complete narcosis with loss of the spinal cord reflexes. The medulla is affected only very late, when respiratory paralysis ensues, and the heart remains active even after respiration has ceased. The great proportion of the æther is rapidly excreted in the pulmonary tissues. During their excretion the æthereal preparations are believed to increase the pulmonary secretion, as they certainly do when administered by inhalation. Thus they are useful expectorants.

When injected subcutaneously æther has distinct powers as a general circulatory stimulant. Its action in this respect is obscure, since it is not a direct cardiac stimulant but rather depresses the cardiac muscle.

Therapeutics. *External.*—Since æther is a solvent for fats and waxes it may be used for the removal of these materials from the body, thus the Liquor Saponis Æthereus is useful as a surgical detergent, and for removing the sebaceous secretion of the skin; on this account æther is also used as a solvent and vehicle for more active remedies intended for skin medication or for absorption by the skin: thus æthereal tinctures of iodine, menthol and belladonna are in use. Similarly æther is a suitable solvent for

plugs of cerumen in the external ear; these are rapidly softened and may then be removed by syringing with an alkaline medium.

As a local anæsthetic, by refrigeration of the surface of the skin, æther, employed in the form of a spray, is occasionally useful in minor surgical operations where the hard frozen surface is sometimes of advantage. It should be remembered, however, that although little or no bleeding takes place at first, the subsequent dilatation of the vessels on thawing often leads to considerable hæmorrhage. The process of freezing is somewhat slow, but on this account is less painful. Methylated æther is preferable to pure æther for refrigeration. Æther may also be used to diminish the local pain of neuralgia, and has been injected, 3–5 min. (18–30 cl.), combined with cocaine, into the sciatic nerve in the treatment of sciatica; it is probable that in the successful cases recorded the æther never reached the nerve. If æther be injected into a nerve trunk it causes death and extensive degeneration of the nervous tissue, hence the method cannot be recommended.

Internal.—As a local anæsthetic in the mouth æther has few advantages; since the anæsthesia is superficial, it may be employed for opening small abscesses. Administered in the form of the spirits it is a rapid diffusible stimulant and is used in collapse, syncope and shock from hæmorrhage or injury, as well as in palpitation of gastric origin. As carminatives these preparations are of considerable value in the treatment of flatulent dyspepsia of the nervous type. They are also efficacious in relieving nervous gastralgia, colic and the pain and nausea consequent on gastric irritation; they are besides satisfactory flavouring agents for more active drugs, and cod-liver oil may be rendered more pleasant to take by the addition to it of a little Spiritus Ætheris Compositus. As an antispasmodic æther has been given internally and by inhalation in the treatment of motor hysteria, asthma and croup. Its preparations have occasionally been employed for tape-worm; they have, however, no advantage over the usual remedies for these parasites. As sedative expectorants, the spirits of æther are useful adjuvants in treating bronchitis and other pulmonary complaints. Hypodermic injections, 20–60 min. (12–36 dl.), of æther have proved successful as stimulants in cardiac failure, in typhoid fever, pneumonia and dyspnœa.

Æther (B.P., U.S.P.). $(C_2H_5)_2O$. Characters, colourless volatile liquid, odour characteristic. Sp. gr. 0·720; boiling point 34°–36° C. Contains 92 per cent. volume of ethyl oxide.
Dose: 15–30 min. (1–2 ml.) repeated; 45–60 min. (3–4 ml.) single.

(*a*) Spiritus Ætheris (B.P., U.S.P.). Æther 1, alcohol 2 parts. Sp. gr., 0·802–0·806.
Dose: 20–40 min. (12–25 dl.) repeated; 60–90 min. (4–6 ml.) single.

(*b*) Spiritus Ætheris Compositus (U.S.P., B.P.C.). Hoffmann's anodyne.
Dose: 20–40 min. (12–25 dl.) repeated; 60–90 min. (4–6 ml.) single.

(*c*) Mistura Ætheris cum Ammonia (B.P.C.). Equal parts spirit of æther and aromatic spirit of ammonia.
Dose: ½–1 fl. oz. (15–30 ml.).

Æther Purificatus (B.P.). Characters, colourless volatile liquid with characteristic odour. Sp. gr. 0·720–0·722.

(*a*) Syrupus Ætheris Compositus (B.P.C.). 1 in 50.
Dose: 1–2 fl. dr. (4–8 ml.).

Æther Methylatus (B.P.C.). Characters, those of æther. Sp. gr. 0·717–0·730.

(*a*) Liquor Saponis Æthereus (B.P.C.).

(*b*) Liquor Saponis Antisepticus (B.P.C.).

Acetic Æther

Pharmacology and Therapeutics.—Acetic æther or ethyl acetate possesses actions similar to those of æther. It is a diffusible general stimulant, antispasmodic and carminative. Its advantages over æther lie in its pleasant aroma and taste. It has been used in cases of collapse, etc., and occasionally in mild fevers as a diaphoretic. An inhalation containing ½ fl. dr. in 20 fl. oz. (0·3 per cent.) of tepid water is a useful means of treating laryngeal catarrh.

Æther Aceticus (B.P., U.S.P.). CH_3COOH, C_2H_5. Characters, colourless liquid, fragrant odour and taste. Sp. gr. 0·900–0·907; boiling point 73·9–77·8° C.
Dose: 15–30 min. (1–2 ml.) repeated; 45–60 min. (3–4 ml.) single.

Ethyl Chloride

Pharmacology and Therapeutics.—Its low boiling point renders ethyl chloride a particularly rapid and penetrating local anæsthetic for minor surgical practice and for relieving the pain of neuralgia. Care must be taken in its use, however, as, if the part be long subjected to the action of the spray, sloughing may occur of the frozen tissues. In practice the fine spray from the nozzle of the container is simply directed on the part to be anæsthetised from a distance of from six to eight inches till the part becomes blanched. It is better previous to its use to remove fatty materials from the epidermis by washing with æthereal soap. For the treatment of spasmodic conditions, *e. g.* epilepsy, asthma, croup, etc., glass capsules

containing 5 min. are employed for inhalation. When used as a general anæsthetic, the material must be as pure as possible; it is pleasant to take, rapid in action, and if administered with care causes few after-effects. It is, however, not free from danger and should not be employed as a substitute for nitrous oxide. The respiration must be carefully observed.

Ethyl Chloridum (B.P.). C_2H_5Cl. Characters, gaseous with pleasant odour, but under pressure forms a colourless fluid with a burning sweet taste. Sp. gr. 0·931; boiling point 12·5° C. Supplied in glass vessels with spring capped apex.

Ethyl Bromide

Pharmacology and Therapeutics.—Externally ethyl bromide in the form of a spray is an efficient local anæsthetic, acting by its refrigerant properties. It may be applied directly to the painful spots of neuralgia, or in frontal headache, either as a paint or by a piece of lint soaked in the material, or in the form of a liniment. In the last instance it may be combined suitably with the liniment of menthol. Glass capsules containing 5 min. of ethyl bromide when broken and the vapour inhaled often prove efficacious in the treatment of spasmodic affections, such as asthmatical attacks, epileptiform and hysterical convulsions and nervous headache or migraine. As a general anæsthetic by inhalation it is occasionally of use in short operations; its effects are not prolonged, the induction of narcosis and recovery being rapid.

Ethyl Bromidum. C_2H_5Br. Characters, colourless neutral liquid with æthereal odour and sweetish warm taste. Sp. gr. 1·455; boiling point 39° C. Soluble in water (1 per cent.), alcohol and ether.

Ethylene Dibromide is decidedly poisonous and weakens both the heart and respiratory system. Its sole claim to importance is its efficacy in diminishing the frequency and severity of epileptic seizures.

Ethylini Dibromidum $C_2H_4Br_{22}$. Characters, heavy colourless liquid, characteristic odour. *Dose:* 1–2 min. (6–12 cl.) in almond oil or in gelatin capsile.

Ethyl Iodide

Pharmacology and Therapeutics.—Ethyl iodide is of no use as a local anæsthetic, but if applied as a paint to the surface of the skin the iodine is absorbed and rapidly saturates the body. It is a useful antispasmodic, particularly in spasmodic asthma, croup and whooping cough, and satisfactorily relieves the dyspnœa of asthma and œdema of the larynx. From its large content of iodine it may be given internally or inhaled (glass capsules 5 min.) to saturate the system with iodine in the treatment of rheumatism and syphilitic conditions, particularly of the respiratory tract. Its use in laryngeal tuberculosis has not proved successful. When inhaled it tends to increase bronchial secretion and act as a sedative expectorant, hence it may be employed in bronchitis, etc.

Ethyl Iodidum. C_2H_5I. Characters, colourless liquid with æthereal odour and pungent taste. Sp. gr. 1·943; boiling point 71° C.

Acetone

Pharmacology.—Acetone is a solvent for fats, resins, waxes and for cantharidin, pyroxylin, and celluloid. It is antiseptic; it inhibits the growth of anthrax spores and is a suitable disinfectant for the skin. When applied to the skin, mucous membranes or raw surfaces, it acts also as a hardening agent, astringent and slight rubefacient, while towards fœtid discharges it is powerfully deodorant. Acetone when given internally by the mouth closely resembles alcohol in action, although its toxicity is higher. If injected subcutaneously comparatively large doses have caused little effects on animals; but if the dose be increased narcosis results and the elements of the blood and the kidneys undergo degenerative changes. Inhalation of acetone leads to glycosuria of obscure origin, but it is probable that it is due to deficiency of oxygen, since if a sufficient supply of oxygen be ensured, glycosuria does not occur. Acetone is a constituent of the normal urine and is also exhaled in the lungs; probably it is formed mostly as a result of defective fat metabolism, and a diminution of carbohydrate food increases its amount. Normally fats are completely decomposed into carbonic acid and water, but, in absence of carbohydrate or with other abnormal diet, the fat metabolism stops short at the formation of hydroxybutyric acid, and this by oxidation forms aceto-acetic acid and acetone. These changes are brought about by enzyme action. An increase above the small normal amounts of acetone excreted is referred to as acetonuria; this may occur as a result of inanition, fevers, gastro-intestinal derangements, nervous and mental disease and diabetes; in all of which conditions an entire or partial deficiency of carbohydrates in metabolism is the underlying cause, and therefore the administration of carbohydrates diminishes these forms of acetonuria.

Therapeutics. *External.*—Acetone is a useful menstruum for the preparation of solutions of pyroxylin and cantharidin. Its principal use is, however, as an antiseptic. A solution of iodine in acetone (1 in 50) is employed as a

sterilising agent for catgut. Its disadvantage lies in the irritating fumes of iodo-acetone which are given off. A stronger solution (2 in 5) has been used in the treatment of boils. As an antiseptic for the skin and hands before operations, acetone has considerable advantages; it hardens the skin, and—without previous washing with soap and water—the application, by rubbing with a piece of flannel for four to five minutes just before operation, of a mixture of equal parts of acetone and absolute alcohol destroys the bacteria in the superficial layers of the integument. The action depends partially on the alcohol, but the acetone assists the penetration by dissolving the fats and extracting water. After the acetone treatment it is recommended to apply a little dilute Tinct. Benzoini Co., which by forming an impenetrable layer ensures that no deep-seated bacteria will escape. The method is particularly applicable in midwifery practice, and from its saving of time it may be of advantage in emergency cases. On account of its mild rubefacient effects, a liniment of equal parts of acetone and olive oil has been employed as a local application in rheumatism; but there is no evidence of its superior efficacy.

The treatment of inoperable uterine carcinomata with acetone has given good results in the hands of several authorities since it was introduced by Gellhorn. The treatment is carried out by placing the patient in the Trendelenburg position and pouring into the vagina through a Ferguson's speculum about an ounce of acetone, leaving it in contact for 10 to 20 minutes; after its removal the vagina is swabbed and a glycerin tampon introduced: the treatment should be repeated at intervals of 2 to 3 days or longer. In order to protect the vagina and vulva from the hardening effect of the acetone they may be coated with vaseline. Curetting of the carcinoma to remove dead tissue previous to application is often of advantage. The treatment is not curative; acetone merely hardens the tissues and thus probably delays their proliferation. The application is in itself painless but it does not relieve the pain of the condition; on the other hand, hæmorrhage and discharge are checked, the fœtor of the discharge eliminated, and the patient's life rendered more endurable and in some cases prolonged. The degree of success varies, of course, with the malignity of the tumour, but it is worthy of trial in all inoperable cases and might even be extended to septic cancerous ulcers of the breast.

Internal.—Acetone has no important field in internal therapy. In the hope that it would act as an antiseptic during excretion doses of 5–15 min. have been given in pulmonary tuberculosis. It has been advised and combined with valerian also in the treatment of neuralgia, dyspnœa, and spasmodic conditions, but it cannot be recommended with any confidence. Its use as an anthelmintic for tape-worm is limited and as an inhalation it has a restricted application in asthma and hay fever.

Acetonum (B. P.). CH_3COCH_3. Character, colourless volatile liquid with æthereal odour and camphoraceous taste. Sp. gr. 0·796; boiling point 56·5° C.
Dose: 5–15 min. (3–10 dl.).

Aldehyde, Acetaldehyde

Pharmacology.—Aldehyde, or better acetaldehyde, is an oxidation product of ethyl alcohol. It is mildly antiseptic and irritant and in contact with blood forms methæmoglobin. Given internally it irritates and corrodes the alimentary canal and large doses lead to arterio-sclerosis, nephritis and perhaps cirrhosis of the liver. It is not uncommonly present in cheap alcoholic drinks. When inhaled the vapour of acetaldehyde causes irritation, spasm of the glottis and coughing with a feeling of suffocation; if continued there follows nervous excitement, then depression, and finally narcosis with death from paralysis of respiration.

Therapeutics.—Acetaldehyde is seldom employed in medicine. Occasionally in the form of dilute aldehyde (15 per cent. in alcohol) it is used as an antiseptic inhalation for nasal catarrh and ozæna. For this purpose a 1 in 1000 solution of the dilute aldehyde is employed.

Aldehydum CH_3CHO. Characters, colourless volatile liquid with suffocating odour. Sp. gr. 0·788; boiling point 21° C.

Formaldehyde, Liquor Formaldehydi

Formic aldehyde is a gas which is not obtainable in pure form. It can be produced by distillation from calcium formate or by passing the vapour of methyl alcohol over coke heated to redness; unoxidised methyl alcohol is distilled off and the solution concentrated to contain about 37 per cent. of formic aldehyde. Attempts to concentrate the solution further result in polymerisation and the formation of paraform.

Pharmacology.—Formaldehyde is a powerful antiseptic and in strengths of 1 : 1000 to 1 : 2000 is definitely toxic to bacteria. It possesses the power, in very dilute form, of coagulating albumen, but it also acts on proteins so as to prevent their coagulation on heating; further it delays or prevents the action of ferments on proteins, and added to milk it prevents the coagulation of casein by rennet. These actions have been ascribed to its reduction and combination with amino groups of the proteins. As a disinfectant

it is not so powerful as corrosive sublimate nor even so active as phenol. In the form of a gas it is an efficient room disinfectant in the presence of water vapour; this should not be attained by evaporating the solution of formalin, but by sprays, since during evaporation the formaldehyde is polymerised into paraform which gives off formaldehyde very slowly. The addition of glycerin prevents this, but its evaporation leaves the rooms sticky. In the disinfection of rooms its penetrative powers are not great, but it has the advantage that it does not damage books, oil paintings, clothing, or ordinary fabrics. The Rideal-Walker coefficient of formalin (40 per cent.) is 0·33, that is, it has about one-third the efficiency of pure carbolic acid. Since it acts in the presence of water vapour, the amount of the latter must be arranged so as to give the maximum efficiency with the formalin; if the amount of steam admitted into the room be too great the dilution may be too weak, while if too little steam be admitted then part of the formaldehyde remains inactive as a disinfectant. This will indicate the advantage of using a spray of a known strength of formalin rather than fumigation or vaporisation in the presence of steam.

When applied to the skin or mucous membranes in strong concentration, it is irritant, caustic, styptic, and hardens the skin and tissues, hence its use in histology. The action in many respects is similar to that of tannic acid, being a form of "tanning." Injected in 1 per cent. solution it is used for the preservation of cadavera. The irritant action of formalin on the skin limits its application as a wound antiseptic. Formalin is an efficient anhidrotic and possesses also deodorant properties.

The vapour if inhaled is powerfully irritant, it causes an unpleasant pungent or pricking sensation in the nose and a feeling of rawness in the mouth and throat. Reflexly from irritation salivation ensues and continued inhalation of the gas leads to lacrimation, coughing and bronchial catarrh. In dilute form the gas is mildly antiseptic and deodorant towards the lungs.

Administered by mouth in dilute solution its action on proteins is exerted on the food and on the walls of the stomach and intestines; stronger solutions are definitely irritant, they cause pain in the stomach and often vomiting, while if the dose be not removed severe abdominal irritation ensues, followed by vertigo, narcosis and coma; in concentrated form it is caustic. Owing to the fact that it diminishes the digestibility of proteins it is not a suitable preservative for flesh, milk, etc.; not only so, but as stated above formalin also inhibits the action of enzymes very rapidly.

If it is injected into animals in dilute solution, it produces dyspnœa and convulsions with opisthotonus, respiration is often accelerated and the heart slowed although blood-pressure rises which would point to a stimulant action on the medullary centres. Where the dose has not been fatal formalin is excreted in the urine, mostly as formic acid, but partially as formaldehyde. When added to blood it causes a destruction of the red blood corpuscles and converts hæmoglobin into methæmoglobin.

Therapeutics. *External.*—The principal use of formalin is as an external disinfectant. For the disinfection of rooms various forms of apparatus are in use. These may be grouped in three divisions: (*a*) those in which the formalin is vaporised at ordinary temperatures; (*b*) those in which the formaldehyde is vaporised along with steam by the aid of heat; and (*c*) those in which the formaldehyde is liberated from paraform by heating.

(*a*) Of apparatus for the vaporisation of formalin the Equifex may be taken as a type. In this spray, air and the disinfectant are forced by means of a pump through two tubes, the jets from which impinge on each other and produce a fine spray. As a disinfecting fluid solutions of formaldehyde varying from 0·5 per cent. to 2·5 per cent. are employed and the vapour is directed against the surface to be disinfected. An experienced operator and reliable apparatus are essentials for success.

Formaldehyde may also be evolved by the action of potassium permanganate on formalin. For this purpose formalin is placed in a pail and half its weight of permanganate added; 16–20 oz. of formalin and 8–10 oz. potassium permanganate suffice for 1000 cubic feet. During the chemical action a considerable amount of heat is generated. The room must be hermetically sealed and the gas allowed to act for 12–24 hours. There should be no fire or open light in the room as the gas evolved is slightly inflammable.

(*b*) The typical apparatus for the evolution of formaldehyde by the aid of heat is that of Trillat. An ordinary steam autoclave heated by gas is charged with a solution of formaldehyde with calcium chloride (Formochloral). When sufficient steam pressure is raised, the vapour is allowed to escape by means of a fine jet; the whole apparatus is placed outside the room and the gas permitted to enter the room by passing the jet through the key-hole. The object of the addition of calcium is to prevent polymerisation of the formaldehyde. Half a pint of formalin is sufficient for 1000 cubic feet The same effect may be obtained by evaporating the formalin (30 parts) to which glycerin (10 parts) and water (60 parts) have been added.

In Lingner's steam disinfecting apparatus a

fine spray of vapour is projected at a fairly high temperature. The method is used largely in the disinfection of schools on account of its efficacy and moderate cost.

(c) Paraform, a polymer of formaldehyde, sublimes in presence of heat and combines with the products of combustion to form formaldehyde. It is supplied in the form of tablets which are used with the Alformant lamp. The Alformant or Schering lamp consists of a methylated spirit lamp having over it a metal chimney, which in turn supports a perforated metal cap; in this latter the paraform is placed. 100 gm. of paraform are required for every 1000 cubic feet, and six hours' exposure are required for disinfection. The method is somewhat expensive. A modification, dispensing with the lamp, consists in burning paraform incorporated with carbon; as the latter burns the former is volatilised.

The irritant vapour of formalin may be removed from a room by ammonia, which forms inodorous hexamethylenetetramine.

Besides its use as a disinfectant vapour 10 per cent. strengths of formalin are employed as disinfectant washes for floors, walls, etc.; a 4 per cent. solution of formalin is a suitable preservative for museum specimens, cadavera, and as a hardening agent for tissues. Weaker solutions 1–2 per cent. may be employed as general antiseptics in the sick-room, for washing the hands, sterilising instruments, and for hardening catgut, while 10 per cent. solutions disinfect excrement; the objections to its use are its irritant vapours and its power for hardening the skin; it has even produced inflammation of the nail bed. On account of its antiseptic and stimulant powers, 10 per cent. strengths of formalin have been used with benefit in the treatment of alopecia, ringworm, lupus and dry eczema; formalin 1 in 3 of glycerin is a useful paint in such cases while a single application of ordinary formalin by a brush often cures ringworm. The treatment of inoperable cancerous ulcers and epitheliomata with formalin has been advised; 2–5 per cent. solutions of formalin were applied as compresses to the surface of the growth and induced a superficial necrosis and exfoliation without causing pain, and acted as deodorants; 50 per cent. strengths and over have been employed as caustics for epitheliomata. As formalin-gelatin (Glutol) and lysoform, formaldehyde may be used as a dusting powder for wounds, ulcers and burns. These powders are non-irritant and slowly evolve formaldehyde in contact with living tissues. Painted on the feet in concentrated form or as a 1 per cent. lotion formalin is an excellent deodorant and anhidrotic, hardening the skin also and diminishing the tenderness of the feet. Similarly it efficiently cures soft corns, and for this purpose, as well as for removing warts and polypi, the 37 per cent. liquor is employed; a 10–50 per cent. ointment has been found of service for chilblains. As a douche for the vagina and uterus, and injections for gonorrhœa, strengths varying from 1 : 1000 to 1 : 50 may be used, and in acute or chronic endometritis a 50 per cent. solution has been introduced momentarily into the uterus and rapidly washed out again, or a 1 in 3 solution applied by a probe to the interior of the cavity.

Internal.—As mouth washes ½–1 per cent. solutions of formalin are useful disinfectants and deodorants; the same strength or less made up with glycerin as a gargle is of considerable value in the treatment of stomatitis and tonsillitis, and as a paint or spray in ozæna, diphtheria and laryngeal papillomata. Inhalation of formaldehyde vapour may be employed for nasal catarrh. Tablets are prepared containing formalin and peppermint oil for the treatment of tonsillitis, pharyngitis and laryngitis; their content of formalin is, however, too small for any efficient disinfectant action to take place unless they are taken in sufficient quantities to irritate the mucous membrane. Inhalation of the vapour of formalin has been recommended in the treatment of phthisis; 10 drops of a solution containing 2–5 per cent. with chloroform, menthol, pine oil, and alcohol are inhaled from cotton wool every half hour; the results of the treatment have been encouraging in several instances. Intravenous injections of formaldehyde have been given in phthisis with, it is stated, beneficial effects; 50 c.c. of a 1 : 2000 solution of formaldehyde (1 in 800 formalin) with a 1 : 4000 solution of chinosol have been used.

Aldehydum Formicum, Formaldehyde. HCOH. A colourless gas.

Liquor Formaldehydi (B.P.). Formalin 36–38 per cent. formaldehyde in water. Characters, colourless liquid with pungent odour and caustic taste. Sp. gr. 1·08.

(*a*) Collutorium Formaldehydi. Formalin 4 per cent. with oil of peppermint, alcohol, and peppermint water.
Dose : a few drops in half a tumblerful of water as a mouth-wash.

(*b*) Gargarisma Formaldehydi. 1 of formalin in 500.

(*c*) Tabellæ Formaldehydi. Contain ½ min. of formalin.

Lysoform

A liquid formaldehyde potash soap.

Special Therapeutics. — Comparatively non-poisonous but highly antiseptic and does not

coagulate albumen. It is used in 2–5 per cent. solution as a general antiseptic for surgical purposes, and ½–1 per cent. for mucous cavities and abscesses. Ointments of 5–20 per cent. strength with lanolin have given good results in psoriasis, lupus, eczema, impetigo, alopecia areata and other skin diseases, while dusting powders may be employed for moist eczemas, burns and ulcers. Lysoform is an efficient antiseptic, the soap it contains acting also as a cleansing agent.

W. J. D.

THE ACTION OF ANÆSTHETICS

Only the anæsthetics in general use will be dealt with, viz. Nitrous Oxide, Ethyl Chloride, Ether and Chloroform, with a passing reference to those which are but rarely employed, such as ethyl bromide, methyl chloride and "methylene." Ethyl bromide and methyl chloride are contained with ethyl chloride in "Somnoform" which is not much used. The proportions are ethyl bromide 5, methyl chloride 35, and ethyl chloride 60 parts, but most anæsthetists prefer the use of chloride of ethyl alone. Ethyl bromide has been employed for short operations such as the removal of adenoids, but it too has almost fallen into disuse. "Methylene," obtained by the action of metallic zinc on chloroform and alcohol, was at one time thought to be bichloride of methylene, CH_2Cl_2, but it is probably a mechanical mixture of methyl alcohol and chloroform, *i. e.* a dilute chloroform, and its action resembles to some extent the last-mentioned anæsthetic. For some years it was largely employed, but has gradually dropped out of use.

The only anæsthetics officially recognised are chloroform, ether and ethyl chloride.

Chloroform, $CHCl_3$, may be prepared from ethylic alcohol, industrial methylated spirit, or acetone, by heating with chlorinated lime, slaked lime and distilled water, subsequently purifying and adding 2 per cent. absolute alcohol. Sp. gr. 1·483 to 1·487. The B.P. 1914 has therefore rendered official the three distinct products which have been in use for some years, viz. that (1) from ethylic alcohol, (2) from "methylated spirit" and (3) from acetone. The first two appear to be identical—chemical analysis and clinical results showing no difference—but acetone chloroform differs slightly clinically and chemically from that prepared from alcohol. Wade found the difference to depend upon a small percentage (0·25 per cent.), of ethyl chloride which is contained in chloroform prepared from alcohol but which is absent from the acetone product. Some dealers add the necessary amount of ethyl chloride to acetone chloroform before putting it upon the market. The B.P.C. states that the three products cannot be distinguished during use.

Æther, or ethylic ether $(C_2H_5)_2O$, may be obtained by distilling a mixture of ethylic alcohol or industrial methylated spirit and sulphuric acid, and rectifying the distillate. Sp. gr. 0·720. As is the case with chloroform, the B.P. 1914 has placed the official seal upon ether obtained from methylated spirit as well as upon that from ethylic alcohol. The liquid used for producing general anæsthesia is Æther Purificatus, which also has a sp. gr. 0·720 and has been freed from all methyl compounds. It may have been obtained from either of the above sources, but when inhaled these two products do not apparently differ pharmacologically. (Methylated ether, used externally for producing local anæsthesia and for cleansing purposes, must never be employed as a general anæsthetic and must not be mistaken for the above "anæsthetic ether" obtained from non-dutiable "methylated spirit.")

A. C. E. mixture should consist of (Vapor Chloroformi Co.) alcohol 16, chloroform 32, and purified ether sufficient to make 100 parts.

Ethyl Chloride, C_2H_5Cl, is now official, having been introduced into the B.P. 1914, which states that it may be obtained by the action of hydrochloric acid on ethylic alcohol or on industrial methylated spirit; in the latter case it will contain a small but variable proportion of methyl chloride CH_3Cl. Only a purified liquid should be employed for producing a general anæsthesia and never the liquid used as a local anæsthetic by freezing.

Nitrous Oxide, N_2O, has no official method of preparation, but may be obtained by heating ammonium nitrate. It is a gas, but is conveniently contained in liquid form in iron bottles under pressure.

Anæsthetics are described as substances which abolish sensation, but as other drugs—narcotics, etc.—will produce this effect a further definition is required. Natural sleep is much more profound in some individuals than in others, and the effect upon the nervous system of light slumber, deep sleep, a hypnotic, a narcotic, and an anæsthetic, appears to be a matter of degree. A narcotic, when given in a sufficient dose, shows the same stages in its action as those produced by an anæsthetic, but its action is so prolonged and cannot be regulated with the nicety required during the administration of an anæsthetic for a surgical operation that it cannot be classed as an anæsthetic. Sir Frederic Hewitt gives seven postulates required by drugs before they can be grouped as anæsthetics.

The action of the various anæsthetics is generally considered as demonstrating four stages—

1. The stimulating.
2. The narcotic.
3. The anæsthetic.
4. The paralytic.

There is no dividing line between these stages, which gradually merge into one another, but they are best seen when anæsthesia is slowly induced, as with chloroform or ether. Nitrous oxide and ethyl chloride are so rapid in their action that the stages are very short and not so easily demonstrated, although they can be distinguished.

1. In the first stage, as its name implies, the functions are stimulated. Respiration becomes deeper and sometimes quicker, the heart improves in force and frequency, the secretions are stimulated and cerebral hyper-activity may be remarked upon by intelligent patients as the vapour is inhaled. Consciousness is retained during this stage, but is gradually weakened and is lost as—

2. The second stage is entered. During this stage the patient is unconscious, and the reflexes, as the administration is continued, one by one disappear, the coarser (*e. g.* the scleral) going early, the finer (*e. g.* the corneal) persisting till later. This stage gradually merges into—

3. The third stage in which not only is the patient absolutely unconscious, but reflexes are abolished. The heart and respiration continue functioning until—

4. The fourth or paralytic stage is entered. When this occurs, as the result of an overdose, respiration usually ceases first, the heart continuing to beat for a short time after breathing has stopped. Absence of the radial pulse must not be taken as indicating stoppage of the heart.

Although these stages were recognised early in the career of anæsthetics, we are yet, more than half a century later, unable to state *precisely* how they act. Investigations have been conducted by physiologists, chemical physiologists, pharmacologists and anæsthetists regarding the effect produced by various anæsthetics upon the heart, the respiration, the blood, the blood-vessels, the blood pressure and the nervous system, but it cannot be stated what is the *exact* nature of the change in the animal organism which produces, with more or less rapidity, a condition of unconsciousness with abolition of reflexes which may be maintained for comparatively long periods, and which, on withdrawal of the vapour, allows of perfect recovery to normal in a short space of time.

The anæsthetic vapour can, in some cases, be demonstrated in the expired air many hours after return to consciousness, and it is generally accepted that the drug is unchanged whilst imprisoned within the animal organism, but Nicloux and Fourquier believe that when it enters the blood, chloroform is decomposed by the alkalies contained therein, with the production of KCl, CO, and H_2O.

When an anæsthetic is inhaled the vapour is absorbed from the pulmonary alveoli by the blood until the tension in both becomes equal. By the blood it is carried to all parts of the body. Moore and Roaf and others suggest that the various anæsthetics enter into a loose chemical combination or physical aggregation with the proteins of the corpuscles and serum, dissociation occurring when the chloroform tension is lowered. The red corpuscles hold between 80 and 90 per cent. of the chloroform in the total blood. The combination apparently does not cause any permanent change in the blood, but Da Costa affirms that after administration of ether there is: (1) a constant diminution of hæmoglobin; (2) that the diminution is rapid and marked, and (3) is accompanied by alteration in shape of the corpuscles, but (4) that there is no diminution in their number. From a short series of cases in which I estimated the amount of hæmoglobin before and immediately after anæsthesia, I was not able to confirm Da Costa's statement.

The *Brit. Med. Assoc. Report* (1911) states that the blood is not deoxidised during anæsthesia, any changes in the proportion of gases which may occur being the result of variations in the thoracic movements and in the volume of the respirations. During chloroform anæsthesia, the blood retains up to the time of death its normal power of taking up oxygen, as shown by Tissot's experiments published in the Report.

Blood absorbs more anæsthetic vapour than serum, and serum more than water, and the Special Chloroform Committee, referring to this fact as well as to the fact that blood delivers less anæsthetic than water under extraction, concludes that blood " does not act as a simple solvent, but rather as a temporary retaining and restraining medium that helps to convert irregular into constant flow " to the tissues. Camus and Nicloux, in investigating the action of ethyl chloride, demonstrated that when administered slowly very much larger quantities could be absorbed by the blood without killing the animal than when given rapidly. These principles undoubtedly govern the action of all anæsthetics, and it has long been recognised clinically than an initial concentrated vapour greatly increases the risk of cardiac failure, and my experiments with ethyl chloride have demonstrated that the higher the percentage

of vapour inhaled the more rapidly does the blood pressure fall.

The blood delivers the anæsthetic to the protoplasm of the tissues with which loose combinations are formed. Investigations support the hypothesis that the greater the amount of lipoids contained in a tissue the greater is the amount of anæsthetic absorbed by that organ. Consequently the nervous system, in which lecithin is largely found, absorbs a large proportion of the anæsthetic carried by the blood, other organs absorbing varying but smaller amounts. The investigations of Camus and Nicloux amply prove this. The theory that anæsthesia is the result of extraction of fat from the tissues can hardly be correct, for it is scarcely conceivable that with the rapid recovery on the withdrawal of the anæsthetic vapour equally rapid reabsorption of the fat occurs. Yet Muskens, in dealing with the after-effects of chloroform, states that he has confirmed Reicher's observation that lipæmia follows narcosis. Meyer and Overton have concluded that the narcotic value of a drug depends principally upon its solubility in lipoid substances and that anæsthetics act through being absorbed by the lipoids in the cells of the central nervous system. Traube agrees that the extent of the solubility of an anæsthetic in the cell lipoids determines its action, but he maintains that the drug must first gain entrance to the cells by surface tension, the difference in which alters the direction and rapidity of the osmosis.

The anæsthetic having gained an entrance to the cell and having formed an unstable or loose chemical compound within it, the chemical action of the protoplasm becomes limited, *i. e.* protoplasmic paresis occurs, and the organ or tissue which contains the largest quantity held by the lipoids suffers most, viz. the central nervous system, with the result that consciousness and the reflexes are abolished, whilst other organs holding less anæsthetic do not completely lose their functions. For example, the kidney continues to secrete urine and the liver bile, but in diminished amount. Bronchial, salivary and lacrimal glands, etc., are not paralysed, as every anæsthetist knows. Rutherford has recently published the results of observations (in 200 cases) of the action of anæsthetics upon the lacrimal gland. He finds "that in the first stage the internal canthi may be wet or dry, in the second stage the lacrimal glands are always active, and in the third stage that the lacrimal secretion ceases at the same time as the earliest reflexes disappear, and that this cessation usually precedes the abolition of the corneal reflex by a very short interval." It is evident, therefore, that all protoplasm is not paralysed to the same degree during anæsthesia, but that organs containing less lipoids and consequently holding a lower concentration of anæsthetic are not so profoundly affected as those with a more abundant supply. Proof that the larger the proportion of lipoids in an organ the larger is the absorption of anæsthetic, and the fact that proportionate paresis or paralysis follows, still leave for solution the questions—How does the anæsthetic cause the paresis? and What is the change effected within the cells?

It has been shown by experimenters that ether, chloroform and allied drugs reduce the oxidising power of living cells, and the theory has been submitted that the temporary paralysis of the cerebral cells, *i. e.*, anæsthesia, is due to diminution of the oxygen-content of the cells. In other words, oxygen and anæsthetic vapour are conveyed by the blood to the central nervous system, the anæsthetic lessens the power of the cells to absorb the oxygen, and the vitality of the cells is so lowered or temporarily paralysed that anæsthesia results.

Heart.—The action of an anæsthetic may be directly upon the organ itself or indirectly through the vagus. That the heart can be profoundly influenced by *chloroform* has been shown by the sudden stoppage which sometimes occurs at the beginning of inhalation when a concentrated vapour has been administered. On being absorbed from the pulmonary alveoli by the blood the first organ to be supplied by the anæsthetic is the heart itself through the coronary arteries, and the effect may be a sudden paralysis of the organ—most probably from the action of the anæsthetic upon the nerve ganglia rather than upon the muscular tissue. This primary cardiac failure is rarely, if at all, seen when the vapour first administered is dilute (0·2 per cent. for children and 0·5 per cent. for adults), and gradually increased in strength. A similar effect upon the heart may be the result of stimulation of the vagus. Vagal inhibition was not found by the Special Chloroform Committee of the British Medical Association to occur when not more than a 2 per cent. vapour of chloroform was inhaled. With a more concentrated vapour the excitability of the vagus mechanism is increased, especially in the early part of the administration.

It has long been stated (from clinical observation) that children bear chloroform well, and although they are, like adults, subject to poisoning by overdose, they probably are more or less exempt from cardiac inhibition from the fact that the cardiac inhibitory fibres seem almost inactive at birth, their tone increasing with age up to twenty-five or thirty-five years.—(Cushny.)

When given as a weak vapour at first and gradually increased to not more than 2 per cent. the initial action of chloroform upon the

heart is one of stimulation and later of depression, but when the various stages are normally passed through and anæsthesia results, if an overdose is given the heart does not stop beating for a short time after respiration has been paralysed. It may be taken, therefore, as a general rule that if chloroform, *per se*, produce primary cardiac failure it will be early in the administration, if cardiac failure occur later it will be secondary to respiratory causes.

In my experiments with *ethyl chloride* I showed that its initial action upon the heart is one of stimulation, which rapidly passes off, the subsequent effect being one of cardiac weakening and dilatation, the appearance of which is earlier the more concentrated the vapour. The heart itself is directly affected, as also proven by Embley and by Webster. My experiments led me to the conclusion that the ventricle is affected before the auricle, the latter suffering more than the ventricle at a later stage.

Cardiac paralysis follows that of respiration, and in one of my experiments in which the heart had ceased to beat, recovery occurred after forcible inflation of the lungs several times by blowing into the tracheal tube. Ethyl chloride does not paralyse the vagus.

Ether has been shown, both clinically and experimentally, to be devoid of the ill-effects of chloroform and of ethyl chloride upon the heart, and unless the strength of vapour inhaled be large, cardiac paralysis does not occur. It is always secondary to respiratory paralysis. Embley found during his experiments that cardiac inhibition may occur when the blood pressure is lowered by a strong vapour, but "a sound heart, however, soon escaped from inhibition, permanent arrest in such cases never occurring," ether rapidly depressing the vagus mechanism. He also found that "the percentage of ether present in the blood of dogs killed by an overdose of ether is not sufficient to produce any effect upon the isolated heart." Binz affirms that the healthy heart, if the amount of ether administered is not too large, is unaffected except that at first its action is stimulated, but that death can result from paralysis of the respiratory centre. Embley found that with 10 per cent. ether vapour the heart was quickened, with 15 per cent. it was unaffected, and with 20 per cent. and upwards it was always slowed. In one of my experiments I showed that ether had a markedly stimulating effect upon a heart depressed by ethyl chloride. Others, both clinically and pharmacologically, have obtained similar results, showing that ether as administered in surgical practice is free from any direct cardiac, paralytic or depressant, action.

Nitrous Oxide depends for its action neither upon its decomposition into its constituent elements with consequent hyperoxygenation of the organism, nor upon its withholding oxygen (asphyxiation). It has a true anæsthetic action, and its deleterious effects appear to be due entirely to intercurrent asphyxia. Wood and Cerna, in their experiments upon dogs, found that inhalation of the undiluted gas slowed the heart and increased the volume of the pulse from stimulation of the vagus. Binz, on the other hand, in his researches administered the gas to one of his assistants and found that the pulse became somewhat more frequent and fuller. Equally divergent observations are made by other observers. Nitrous oxide has a stimulating action upon the heart, and any untoward effect upon this organ is secondary to respiratory embarrassment (asphyxia), causing engorgement of the right heart. For this reason a second administration of the gas should not be proceeded with until the patient has been allowed to recover *completely* from the first. That this cardiac effect is asphyxial in origin is demonstrated by its diminution or prevention when oxygen is given with the gas. Cardiac dilatation has been observed on administration of a mixture of "gas and oxygen," and a warning is issued that this mixture should never be followed by inhalation of chloroform. A safe anæsthesia can be maintained by the mixture of nitrous oxide and oxygen for considerable periods. My own clinical experience has been in administrations for varying periods up to thirty-five minutes. Claude Martin has proven its safety by keeping a dog anæsthetised with it for seventy-two consecutive hours, complete recovery occurring within a few minutes of withdrawal of the anæsthetic vapour.

Respiration.—If we except the irritation of the respiratory tract the action of anæsthetics is upon the respiratory centre. It has been shown that cardiac arrest may occur with a high percentage of chloroform vapour in the first stage, but having safely passed that danger with the induction of anæsthesia, an overdose of any of the anæsthetics causes respiratory paralysis before that of the heart. Respiratory rhythm is frequently disturbed—

1. From irritation of the tract by the anæsthetic vapour causing the patient to hold his breath, cough, sneeze, etc.;
2. From nervousness;
3. By struggling (either voluntary or involuntary);
4. By retching or vomiting;
5. By diminution of oxygen or increase of carbonic acid in the blood supplied to the respiratory centre;
6. By too liberal a proportion of oxygen when that gas is given with the anæsthetic;
7. Or during surgical manipulation, *e. g.* traction upon viscera.

The action of the anæsthetics in absence of extraneous causes affecting the rhythm is initially to quicken and deepen respiration from stimulation of the centre. With the rapidly acting anæsthetics this stage is quickly passed through, and chloroform, ethyl chloride and nitrous oxide more quickly depress the centre than does ether. In every instance if "pushed" to the fourth stage breathing becomes slower and shallower, with ultimate stoppage from paralysis. In some of my experiments with ethyl chloride I found that breathing ceased with the chest in the deep expiratory position (an important point in reference to treatment). During administrations in which rebreathing is allowed (closed ether, ethyl chloride and nitrous oxide without valves) the CO_2 rebreathed by the patient stimulates respiration with the more rapid supervention of paralysis due to the double effect of the lethal action of the CO_2 and the larger intake of the anæsthetic vapour. The supervention of cyanosis, therefore, must be regarded as a warning, but its prevention should be always aimed at no matter which anæsthetic is administered.

As respiratory arrest in the fourth stage of anæsthesia under any anæsthetic normally occurs before cardiac failure, the administrator must see to it that breathing is free. With absence of respiratory embarrassment from any cause secondary cardiac failure *due to the anæsthetic* cannot occur.

Blood Pressure.—Fall of blood pressure may be due to diminished force of the heart beat, or to relaxation of the blood-vessels, or to a combination of the two.

Investigations of a very searching character have been conducted with regard to *chloroform* by Hill, Embley and Martin, Sherrington and Sowton, and others. Results demonstrate that in the early stage vaso-constriction occurs, followed more or less rapidly—according to the degree of concentration of the vapour—by dilatation. "In chloroform poisoning the dilatation would appear to be more or less confined to the splanchnic area." (Report of the Special Chloroform Committee, B.M.A.) There is a decided fall in blood pressure, in consequence, which may be increased by the cardiac depression caused by the drug. The fall is more marked in the "feet down" position, as emphasised by Leonard Hill, hence the greater risk of cardiac failure when the patient is given chloroform in the sitting posture.

With *ether* there is not the great risk of fall of blood pressure, but with high percentages lowering will occur, especially when administered by the open method. Embley has confirmed McWilliam's observation that great relaxation of the arterioles occurs with fall of blood pressure. He finds that mild asphyxiation, such as occurs in administration by the closed method, raises the blood pressure, obviating the fall which would otherwise result. Buxton states that blood pressure is increased until very deep narcosis is present, when a slight fall occurs. Kemp also found ether to raise blood pressure.

Ethyl chloride first slightly raises blood pressure, and, except with weak vapours (under 10 per cent.), then depresses it. The depth and rate of fall depend directly upon the concentration of the vapour. I have found the fall to be cardiac in origin, vaso-constriction occurring until a profound stage of anæsthesia is reached. Embley found that vascular dilatation occurred with fall of blood pressure. Webster and Cole have also demonstrated fall of the pressure.

Nitrous oxide raises blood pressure especially, as pointed out by Buxton, in the brain and spinal medulla. Its elevation is greater when the gas is given with valves than when rebreathing is permitted.—(Hewitt.)

Nitrous oxide and oxygen, according to Hill, raises the pressure slightly if at all. Oliver found that this mixture causes a greater rise than did nitrous oxide alone.

By means of his arteriometer Oliver investigated and compared the action of various anæsthetics upon the radial pressure, and showed that ether caused the greatest increase, whilst nitrous oxide and oxygen came next. With N_2O alone he found "a slight expansion, followed by a reduction, either to the normal calibre or to a point or two below it." The arteriometer showed a great diminution in the pressure with chloroform, whilst A. C. E. also depressed it, but not to the same extent as chloroform, as one might expect from the beneficial action of the ether.

Liver and Kidneys.—Nitrous oxide has very little, if any, action upon these organs, but with the other anæsthetics (especially chloroform) symptoms simulating acute yellow atrophy of the liver occasionally occur. In cases ending fatally the liver has been found to be more or less fatty, sometimes of a canary-yellow colour. The kidneys and the heart also show fatty changes. The condition has been found to follow ether administration, and also after ethyl chloride, but with these it is so rare compared with chloroform that the affection frequently goes by the name of chronic, or delayed, chloroform poisoning. The condition resembles an acid intoxication. One of the worst cases we have had in the Ulster Hospital for Children and Women followed administration of ethyl chloride for about one minute and was reported by Cunningham in *The Lancet* (1908). The cause of this acidosis is explained by Francis and Fortescue-Brickdale as follows: "Diminished oxidation processes characterise the action of all the halogen

narcotics; it is supposed that the imperfect oxidation of the body fats gives rise to acids of the fatty series, and hence the production of these symptoms. The action does not apparently depend upon the narcosis, but is a special property of this class of drugs." The halogen cannot be the sole cause of the condition, for it has been reported to have followed the administration of ether, which does not contain a halogen. Nicloux and Fourquier claim that the decomposition which they believe to occur upon the inhalation of chloroform (referred to above), whereby the alkalinity of the blood is diminished, explains the occurrence of acidosis.

Wallace and Gillespie have shown that faulty metabolism is a most important element in the causation of acidosis, especially regarding carbohydrates, and they have demonstrated the usefulness of glucose as a prophylactic. The conclusions to which their investigations have led them are—

"The condition of acid intoxication occurring after an anæsthetic is not primarily due to the anæsthetic, but takes place in those whose metabolism is unstable. Either the glycogenic function of the liver is in abeyance, or the intake of carbohydrates is deficient, or there is present some condition involving the activity of the liver cells which devitalises them. On such condition is superposed the action of an anæsthetic. The combined effect may be one of acidosis, but owing to the rapid elimination of the exciting cause the body may quickly regain its metabolic balance. But if before operation the balance is so faulty that acidosis is present the sequel to the anæsthesia will be an acid intoxication with its possible catastrophe."

Some authorities have suggested sepsis as a cause of the condition, but there is no doubt that it frequently occurs in cases in which sepsis is entirely absent.

Hewitt quotes Offergeld's conclusion that "postponed chloroform death" is due to fatty degeneration of the kidneys. He ligatured the renal artery and found that fatty changes did not occur in the organ after forty minutes' anæsthesia, whereas pronounced fatty degeneration followed ligature of the renal vein and an anæsthesia of thirty minutes.

Glycosuria may be the result of the action of the anæsthetic upon the liver, or possibly upon the pancreas, or upon the medulla oblongata. This question has not been decided. Some experimenters have shown that excess of carbon dioxide may be the exciting cause. Glycosuria may follow administration of ether or chloroform, but generally passes off in a few hours.

The action of an anæsthetic upon the kidney sometimes shows itself in the production of albuminuria which may vary in amount and persistence. Ether may cause it by producing congestion of the kidney, chloroform by setting up cloudy swelling. Many physiologists and anæsthetists have estimated the output of urea and urine. Both are diminished. The amount of urine secreted is stated by some to be increased at the beginning of inhalation and decreased later. The early increase is no doubt a result of the initial stimulant action of the anæsthetic. I have had many opportunities of administering anæsthetics for my colleague, Mr. Fullerton, during cystoscopic examination and catheterisation of the ureters, and the decrease in the flow was found to be such that he has latterly had an anæsthetic administered for such a procedure only when absolutely necessary. The Trendelenburg position is said greatly to decrease the urinary secretion, but the kidney function is not in abeyance, for a good quantity of urine can be frequently drawn off by catheter at the end of a pelvic operation when the bladder had been emptied just before the patient was placed upon the table.

Lungs.—The inhalation of an anæsthetic vapour, especially ether, may so irritate the respiratory tract that its secretion is much increased. This, in some cases, causes cyanosis, in others it does not seem to interfere with the intake of air. This hypersecretion is occasionally followed by bronchitis or pneumonia, but it must not be assumed that every such case is one of "ether pneumonia." "Aspiration pneumonia" or "septic pneumonia" may follow the administration of an anæsthetic. Hypersecretion is not necessarily a forerunner of bronchitis or pneumonia.

Temperature.—Chloroform and ether lower the body temperature, the fall, which has been found to be as much as 2·5° F., being dependent largely upon the diminished oxidation going on within the body during inhalation. The diminution is also influenced by the amount of perspiration, which varies from nothing to a drenching sweat. The extent of surface required to be exposed for the performance of the operation and, in the case of abdominal operations, the cooling and drying of viscera withdrawn from the peritoneal cavity tend to increase the fall of temperature produced by the action of the anæsthetic upon the body.

Muscles.—The vitality of voluntary muscle is depressed before that of involuntary, the apparent exception to this being the heart. But, as pointed out above, the action of chloroform upon the heart is most probably through the ganglia contained therein rather than upon the muscular tissue. Cushny states that "the muscles and nerves are not affected by chloroform or ether when inhaled" and in an animal killed by the inhalation of an anæsthetic the muscles still respond to a stimulus.

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V.G.L.F.

DRUGS AIDING THE EXCRETION OF URIC ACID

In addition to lithium compounds, several organic compounds have been introduced into medicine with the object of aiding the excretion of uric acid. The principle on which their use is based is that in vitro all of them readily dissolve uric acid, and it was thought that in the body they might form soluble salts and thus prevent the deposition of urates in the tissues and even cause the removal of those already deposited. It is doubtful to what extent such an action could be exercised in so complex a fluid as the blood where the ions of sodium are so abundant, and in any case the concentration of any of these so-called uric acid solvents which could be present at any time in the blood must be very small indeed when one considers the relatively small doses administered. On theoretical grounds therefore it appears that the administration of these substances would be quite devoid of benefit, but in practice it is found that certain cases are benefited. The chief substances used as uric acid solvents are piperazidin and its derivatives and thyminic acid, many of which are on the market as proprietary remedies.

Piperazina (B.P.C.) (hexahydropyrazine or diethylene diamine $C_4H_{10}N_2$) is official in the French Codex. It is a colourless deliquescent crystalline substance, very soluble in water, yielding a strongly alkaline solution which quickly decomposes. In vitro it is a powerful solvent of uric acid, many times more so than lithium carbonate. In the blood a 0·2 per cent. solution does not dissolve sodium biurate; such a concentration is not probably attained in life. It is administered in cachets, dose 5–15 gr. (3–10 dg.). It is incompatible with iron salts, quinine, alkaloidal salts, sodium salicylate and spirit of nitrous ether.

Preparations

Granulæ Piperazidinæ (Effervescent) (B.P.C.). (8 per cent.)
Dose : 60–180 gr. (4–12 g.)

Glycero-Piperaz (Piperazin acid glycero-phosphate).
Dose : 2–5 gr. (12–30 cg.).

Benzo-Piperaz, dose 2–5 gr. (12–30 cg.), and Salicyl-Piperas, dose 2–5 gr. (12–30 cg.) are crystalline salts of the base.

Piperazidin Quinate (Sidonal) is a white powder.
Dose : 5–25 gr. (3–15 Dg.).

Dimethyl Piperazidin Tartrate (Lycetol) has diuretic properties.
Dose : 15–30 gr. (1–2 g.).

Ethylene-ethenyldiamine $C_4H_8N_2$ (Lysidine) is supplied in 50 per cent. solution.
Dose : 10–30 m. (6–18 dl.).

Lysidine Bitartrate is a crystalline solid.
Dose : 15–30 gr. (1–2 g.).

These three are used the same way as Piperazin.

New Sidonal, said to be a mixture of three parts of quinic anhydride with one part of quinic acid, is used in the same way and in similar doses as Sidonal.

Piperidina (B.P.C.), Hexahydropyridine $C_5H_{11}N$, obtained by the dry distillation of piperine from pepper or synthetically, is a colourless alkaline liquid freely miscible with water and alcohol.

Piperidinæ Tartras (B.P.C.) is used in the same way as Piperazidin, and is said to be more efficacious. It is administered in cachets or in mixtures.
Dose : 10–15 gr. (6–10 g.).

Piperidine Salicylate is similarly employed.

Acidum Thyminicum (Solurol) a product of the hydrolysis of nuclein, is a brownish-yellow deliquescent powder, soluble in water, yielding faintly acid almost tasteless solution. It is said to have no incompatibles and may be prescribed in tablets or cachets or in solution and has also been administered by intramuscular injection in doses of 2 gr. (12 cg.)
Dose : 5–10 gr. (3–6 dg.). P. H.

DRUGS ACTING ON AUTONOMIC NERVE-ENDINGS

Under this heading are considered the actions of a number of drugs which all owe their activity to their basic or alkaloidal constituents. These alkaloids are distinguished by their discriminating, peripheral action on involuntary muscle and gland cells; the action of some of them mimicking, with more or less fidelity, the effects of stimulating the nerves belonging to one or other of the main divisions of the autonomic system, whilst that of others paralyses such effects in an equally selective manner. The

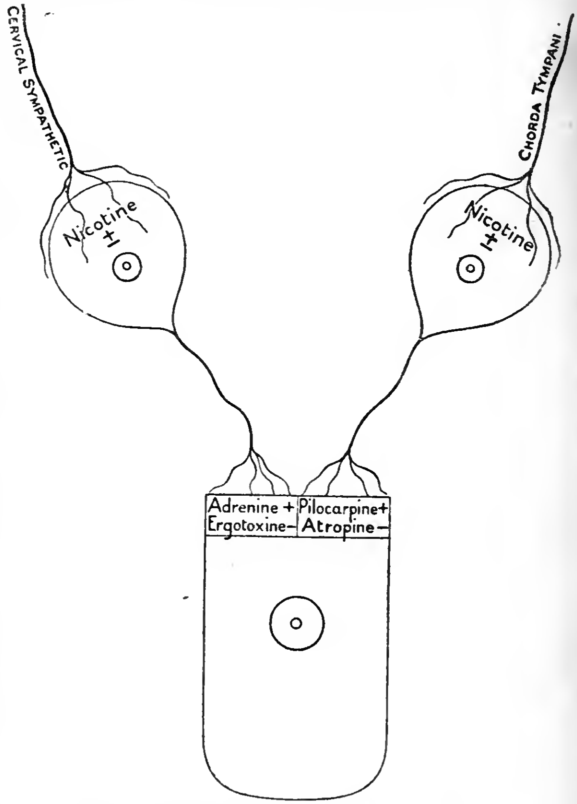
sense in which the term "nerve-ending" is employed may be more conveniently discussed in dealing with the individual alkaloids; but a preliminary word on the classification of autonomic nerves may be useful.

The "visceral," "vegetative" or "autonomic" nervous system supplies nerves to the involuntary muscle and gland cells of the whole body. Each unitary nervous path in the system consists of a medullated fibre of small diameter arising from a cell in the gray matter of the spinal medulla or brain-stem, running to end in contact with a ganglion cell in one of the chains or terminal plexuses into which the ganglia of the system are arranged; from this ganglion cell a second, usually non-medullated, fibre-process arises and ends in the plain muscle or gland cell. The two fibres are known as the pre- and post-ganglionic fibres, and an impulse passing from the central gray matter to a peripheral responsive organ along any fibre of the system encounters only one such ganglionic interruption or cell-relay.

The outflow of fibres from the cerebro-spinal axis to the autonomic ganglia occurs in three regions; there is a cerebral, a thoracico-lumbar and a sacral outflow. In the cerebral outflow are included the branch from the third nerve to the ciliary ganglion, the chorda tympani and Jacobson's nerve, and the vagus (with the accessory); the thoracico-lumbar comprises the pre-ganglionic fibres of the true sympathetic system; the sacral consists of the pelvic nerves or nervi erigentes. In many cases an organ has a double nerve-supply, from the true sympathetic, on the one hand, and from the cerebral or the sacral division of the autonomic system on the other, and the actions of the fibres from the two sources are often reciprocal, one inhibiting where the other is excitatory or augmentor.

The ganglion cells of the whole system appear to be uniform in their pharmacological affinities, and in another section (*Nicotine*, etc.), we shall deal with alkaloids which stimulate or paralyse them all alike. This is not the case with the structures with which the post-ganglionic fibres form terminal connection. We find a series of bases acting on these which reproduce the effects of true sympathetic nerves only, and others which paralyse the action of the latter at the periphery, leaving the function of cerebral and sacral autonomic nerves unimpaired. Alkaloids of another group similarly reproduce the effects of, or paralyse the action of autonomic nerves of the cerebral and sacral divisions only. So that the peripheral connections of the autonomic system exhibit broadly two types of pharmacological affinity, associated with the cerebral and sacral divisions on the one hand, and with the true sympathetic division on the other. Under the different drugs will be discussed the exceptions, and considerations of detail, which blur the outlines of a picture, to which the need for brevity here gives a fictitious sharpness.

The accompanying diagram, representing the double nerve-supply to a salivary gland cell, illustrates the pharmacological affinities associated with the peripheral endings of the fibres from the cerebral and true sympathetic divisions.



The double nerve-supply of a salivary gland cell.

It should be noted that the alkaloid ergotoxine, which should belong to this section, is dealt with for convenience under ergot. In the figure + signifies stimulation, − paralytic action.

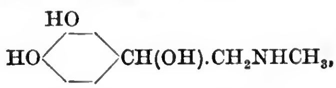
Adrenalin

It has been known since the middle of the nineteenth century that the medulla of the suprarenal gland contains a substance giving a red colour on oxidation, a green colour with ferric chloride, and staining brown with chromates. Smaller masses of similar chrome-staining or "chromaffin" tissue are scattered through the body, always in close relation to ganglia of the true sympathetic system, with the cells of which they are embryologically related.

When Schäfer and Oliver discovered the presence of an intensely active principle in the suprarenal gland, and it was found that this,

like the chromogenic substance, was limited in its distribution to the cells of the medulla, it was suspected that the two might prove to be identical. This was soon found to be the case, and the active principle, after being approximately isolated by Abel, who called it "epinephrin," and by v. Fürth, who named it "suprarenin," was prepared in pure, crystalline condition by Takamine and Aldrich simultaneously, receiving the name "adrenalin" from the former. Since Abel's name "epinephrin" was associated with a conception of the constitution of the principle, now known to be erroneous, the name "adrenalin" passed into general use and has been adopted in the British Pharmacopœia of 1914. In the United States "epinephrin" is the name commonly employed in scientific literature.

The empirical formula of adrenalin, $C_9H_{13}NO_3$, was first correctly determined by Aldrich. By the work of v. Fürth, Pauly, Jowett and Bertrand, among others, the probable constitution was determined as—



or methylamino-ethanol-catechol, and this has been confirmed by the synthesis of the racemic base by Stolz and Dakin, and the resolution of this by Flächer; the synthetic lævorotatory substance being in all respects, chemical and physiological, identical with the natural lævorotatory adrenalin.

The free base, adrenalin, is remarkably insoluble in water, alcohol and all ordinary solvents, and is obtained as a micro-crystalline powder, colourless when pure. The salts, on the other hand, are extremely soluble in water. Like other catechol derivatives, it is very susceptible to oxidation, and neutral or faintly alkaline solutions are rapidly oxidised in contact with air. The pink colour, observed at an early stage of its oxidative decomposition, forms the basis of a number of colorimetric methods suggested for its estimation. In solutions made distinctly acid it is relatively stable, and the 1 in 1000 solutions sold under different trade names all contain some excess of acid.

A series of bases related to adrenalin in structure, with all degrees of closeness, from isoamylamine—

up to the immediate homologues of adrenalin itself, all exhibit an activity of the same general type, the action approaching more nearly to that of adrenalin in intensity and specificity the closer the similarity of structure. Some of its near relatives have been used in therapeutics as substitutes. Another of the series, p.-hydroxyphenylethylamine, is dealt with in the section on Ergot.

The chief feature of the activity of suprarenal extracts described by Schäfer and Oliver, and now known to be due to adrenalin, was the production of a large rise of blood pressure when the extract was injected intravenously, the rise becoming enormous if reflex cardiac inhibition was excluded by section of the vagi or administration of atropine. Schäfer and Oliver found that very small doses of suprarenal substance were enough to produce a maximal rise of arterial pressure, and the isolation of adrenalin has made it possible to appreciate the intense activity of the base. As little as 0·000001 gm. will produce a perceptible rise of pressure when injected intravenously into a rabbit or cat. In the latter animal, when the normal pressure is high, minute doses may cause a fall in place of a rise of pressure.

Schäfer and Oliver showed that the pressor action was due chiefly to peripheral vaso-constriction, to which was added great acceleration and augmentation of the heart-beat if the vagi were out of action. They demonstrated the vaso-constrictor effect on the artificially perfused vessels of the frog, and concluded that the action was a direct one on involuntary muscle. The action which they described on skeletal muscle may have been partly due to other constituents of their extract; but recent work seems to indicate that adrenalin has the power of delaying or removing fatigue of the voluntary muscles.

Later observation (by Lewandowsky, Boruttau, and especially by Langley) showed that the peripheral action is not the same on all plain muscle, but that the action on various organs containing plain muscle or gland cells corresponds to the effect of stimulating the true sympathetic nerve-supply, though it persists when the nerve-fibres have been cut peripherally to the ganglia and allowed to degenerate completely. Brodie and Dixon supplied a negative observation confirming this generalisation; they found that the peripheral pulmonary arterioles, which have no sympathetic nerve-supply, were not constricted by adrenalin. The general validity of the rule, for a large number of organs from different species, was demonstrated by Elliott. Adrenalin has, therefore, a powerful augmentor effect on the activity of all involuntary muscle and gland cells which receive motor fibres from the true sympathetic system. Thus it causes great augmentation and acceleration of the heart-beat, in the absence of reflex vagus control; constriction of all arterioles in the body, with the exception of those of the lungs and brain, in which the vasomotor nerve supply

is deficient; widening of the pupil, retraction of the nictitating membrane, and protrusion of the eyeball; secretion of saliva, tears and tracheal mucus. The pilomotor muscles are but weakly affected, and the sweat glands, in spite of their sympathetic nerve-supply, form an exception in being practically uninfluenced by adrenalin. (See under *Pilocarpine* and *Atropine*.) On the other hand, in organs containing plain muscle which is inhibited by stimulating nerves from the sympathetic system—the stomach, gall-bladder, bowel, urinary bladder (cat), and bronchioles—the plain muscle is likewise inhibited by adrenalin. The action reproduces that of the sympathetic nerves with remarkable precision. Thus, while the muscular walls of the alimentary canal as a whole give an inhibitor response to sympathetic nerve-stimulation or to adrenalin, the pyloric, ileocolic and (in some species) internal anal sphincters are exceptional in receiving motor nerves from the sympathetic system, and they are accordingly excited to constriction by adrenalin. The fundus of the urinary bladder is inhibited in the cat and excited to contraction in the ferret by stimulating the hypogastric (sympathetic) nerves, or by injecting adrenalin. The reaction of the cat's uterus to stimulation of the hypogastric nerves changes from inhibition to excitation with pregnancy, and its response to adrenalin shows a parallel change. It has been mentioned that the action of adrenalin on a tract of plain muscle, though so closely simulating the effect of sympathetic nerve-stimulation, is not reduced by complete degeneration of the post-ganglionic nerve-fibres from that system. On the contrary, the plain muscle appears to become more sensitive to adrenalin under such conditions. This has led Langley, in particular, to the view that adrenalin acts on some constituent of the involuntary muscle or gland cell itself, this constituent being also concerned with the transmission of impulses from sympathetic nerves, but arising independently of the latter.

There are certain poisons which abolish the action of sympathetic nerves and of adrenalin on the muscle, but leave the latter normally responsive to directly acting substances, such as hypophyseal extract or barium chloride. One such is apocodeine. A still more selective paralysant is ergotoxine (see under *Ergot*), which leaves the control by other autonomic nerves unimpaired, and the muscle normally responsive to every kind of stimulus except the motor actions of true sympathetic nerves and of adrenalin. It is necessary, therefore, to postulate the existence of some structure which is not essential for the function of the cell or its response to stimuli in general, but is essential for its response to sympathetic nerve-impulses and to adrenalin. This intermediary mechanism has been called the "myoneural junction" by Elliott. Langley calls it a "receptive substance," in accordance with his general view of the action of poisons. In pharmacological literature it is usual to refer the action to "sympathetic nerve-endings"; and although the term is not strictly defensible on morphological grounds, since true nerve-endings may be expected to degenerate with the rest of the fibre, it is convenient to use it, and not misleading, provided the nature of the convention is explicit. Given a "nerve-ending" or "myoneural junction," which lies on the path of and determines the reaction of the muscle or gland cell to sympathetic impulses, and given that this "nerve-ending" survives the complete degeneration of the nerve-fibres, the action of adrenalin would correspond in all respects to the stimulation of such a structure. The matter has been discussed in some detail, since the expression "nerve-endings" will recur again in describing the relation of the action of pilocarpine and atropine to other divisions of the autonomic system, where it is similarly employed.

The effects of adrenalin described above are characteristically rapid in onset and brief in duration. They are well marked only when the substance is injected intravenously. The evanescence is not merely due to the susceptibility of adrenalin to oxidation, since it may be circulated with little loss through organs, such as the lungs, on which it has little action. The intensity of the action is determined by the excess of adrenalin concentration in the circulating fluids over that in the responsive tissues. When injected subcutaneously, or given by the mouth, adrenalin produces such a pronounced ischæmia of subcutaneous tissue or mucous membrane, that its absorption into the blood stream is extremely slow, and the concentration needed for a pronounced effect is never attained. It must be remembered, however, that adrenalin is a normal constituent of the blood in very low concentration, its secretion from the suprarenal medulla being under the control of the splanchnic nerves, and being necessary for maintaining the tone and efficiency of organs innervated by the sympathetic system. In conditions which deplete the body of its natural adrenalin, the slow absorption from the alimentary canal or tissue spaces may have great value in replacing the natural secretion, without producing the violent, immediate effects of intravenous injection.

In small doses adrenalin has no significant effects other than those simulating sympathetic stimulation. In large doses it produces toxic effects if given hypodermically—glycosuria, albuminuria, necrotic changes in the cells of the liver and kidneys. If a guinea-pig is given a large dose hypodermically it dies with intense

congestion of the lungs and extravasation of blood into the alveoli. There is no evidence of any direct effect of adrenalin on the cerebrospinal nervous system. When it is given in a series of intravenous injections to a rabbit, an atheromatous degeneration of the aorta and large arteries is produced, probably as a result of the repeated high tension to which the vessels are subjected.

Therapeutic Use.—By far the most important use of adrenalin is for the production of local ischæmia of the mucous membranes, or of the subcutaneous or submucous tissues. This action finds direct therapeutic application in removing the congestion of the inflamed conjunctiva or other mucous membrane, and controlling hæmorrhage from small wounds or ulcerations. It is of value, therefore, in epistaxis, bleeding from a tooth-socket, etc., being applied locally in a spray or on pledgets of wool. To bleeding piles it is applied in an ointment or suppository, and for a bleeding gastric ulcer it is swallowed; administration by the mouth being, in this instance, also a method of local application. In hay fever it is used as a spray or as a constituent of a snuff. In solutions for such local application the hydrochloride is usually employed, the proportion being, commonly, 1 in 1000. The free base, which is relatively stable, but also insoluble, is used in snuffs, ointments, medicated gauzes, etc. Apart from such directly therapeutic application, the local action of adrenalin is largely used in surgery for producing a bloodless field of operation in vascular tissues and restricting the absorption of local anæsthetics. For infiltration of subcutaneous and submucous tissues solutions of 1 in 100,000 in saline, with the required proportion of local anæsthetic, are commonly employed. Strong solutions of adrenalin, such as 1 in 1000, are liable to produce local necrosis if given under the skin, on account of the intense and long-persistent local anæmia which they produce.

For its effects after reaching the general circulation adrenalin may be employed with real benefit, but should be used with caution. It is sometimes given intravenously in shock or collapse, but has little value if injected suddenly, the effect being over-violent and very evanescent. For such purposes the dose should be diluted with a large volume of warm sterile saline and slowly infused. In certain forms of heart-failure it can be shown experimentally to revive the beat, even after long cessation, when the heart is stimulated concurrently by massage. In the heart-failure of the early stage of chloroform administration, on the other hand, adrenalin is definitely dangerous, and there is reason to believe that its absorption from highly vascularised tissues, into which it has been injected under light chloroform anæsthesia, has been the determining factor in producing a fatal fibrillation of the ventricle.

Adrenalin is often given by the mouth for hæmoptysis and menorrhagia, though its reputed effect in checking the hæmorrhage under such conditions is not easily explained. It does not, as is sometimes stated, increase the coagulability of blood, if one may judge from observations on the normal subject. Its value in asthma, on the other hand, is not only supported by clinical evidence, but rationally based on its inhibition of the muscular coats of constricted bronchioles. It has occasionally been used to promote the contraction of the atonic uterus after labour, but is unlikely to have the value of hypophyseal extract for this purpose. After acute fevers, especially diphtheria, when the store of adrenalin in the suprarenal glands is much reduced, the administration of adrenalin by the mouth or rectum is of undoubted value. In Addison's disease, on the other hand, no permanent benefit results from its employment.

Preparations

Adrenalinum (B.P.).

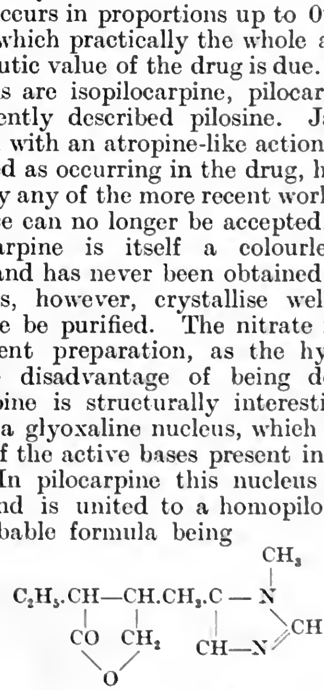
Liquor Adrenalini Hydrochloricus (B.P.). 0·1 per cent.

Dose: 10–30 min. (6–18 dl.).

Pilocarpine

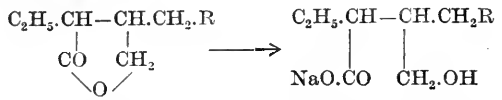
The leaves of *Pilocarpus microphyllus*, and of various related species, contain several alkaloids, of which by far the most active is Pilocarpine, which occurs in proportions up to 0·5 per cent., and to which practically the whole activity and therapeutic value of the drug is due. The other alkaloids are isopilocarpine, pilocarpidine, and the recently described pilosine. Jaborine, an alkaloid with an atropine-like action, which was described as occurring in the drug, has not been found by any of the more recent workers, and its existence can no longer be accepted.

Pilocarpine is itself a colourless, syrupy liquid, and has never been obtained crystalline. Its salts, however, crystallise well, and can therefore be purified. The nitrate is the most convenient preparation, as the hydrochloride has the disadvantage of being deliquescent. Pilocarpine is structurally interesting as containing a glyoxaline nucleus, which occurs also in one of the active bases present in ergot (*quo vide*). In pilocarpine this nucleus is methylated, and is united to a homopilopic radicle, the probable formula being



(Jowett and Pinner).

When alkali is added to a solution of the base the lactone ring is opened and an alkaline salt of pilocarpic acid formed, which is practically inert (Marshall).



This change possibly accounts for the fact that on instillation into the eye, where it mixes with the alkaline tears, a solution of pilocarpine base is less active than a solution of one of its salts.

Action.—Pilocarpine produces most of the effects of stimulating autonomic nerves belonging to the cerebral and sacral divisions of the system, and certain other effects which do not come under this heading. A prominent feature of its action is the stimulation of profuse glandular secretion. The salivary glands, the glands of the buccal mucous membrane, of the trachea, and of the stomach, the pancreas, and probably the glands secreting the succus entericus, are all excited to secretion by this alkaloid. In all these cases, where the paths of nervous control can be identified, the secretion produced by pilocarpine has a marked resemblance to that evokedby stimulating the cranial autonomic nerve-supply. Thus, in the case of the submaxillary gland a profuse flow of thin saliva, accompanied by vasodilatation in the gland, is produced either by pilocarpine or by stimulation of the chorda tympani. In the case of the pancreas, a small flow of thick, viscid juice is produced by pilocarpine, or by stimulation of the vagus. In either case a small dose of atropine promptly abolishes both effects. It is, indeed, a rule to which no exception has yet been discovered, that any effect of pilocarpine is abolished by a relatively small dose of atropine. The case of the sweat glands furnishes an interesting exception to the association of pilocarpine action with innervation by cerebral or sacral autonomic nerves. These glands are innervated only from the true sympathetic system, but their secretion is powerfully stimulated by pilocarpine. This action, as also that of stimulating the nerves, is abolished by atropine.

In its effects on involuntary muscle pilocarpine again reproduces the action of cerebral and sacral autonomic nerves with considerable accuracy. Thus, it causes constriction of the pupil, and contraction of the ciliary muscle, as does stimulation of the oculomotor nerve; powerful peristaltic contractions of the stomach and small intestine, as does stimulation of the vagus; inhibition of the heart-beat, and contraction of the bronchioles, again like vagus stimulation; powerful contraction of the rectum and bladder, like that produced by stimulating the sacral autonomic supply. In all these cases, again, the action of pilocarpine is annulled by atropine, even where, as in the case of the bowel and bladder, the latter alkaloid has but slight paralytic action on the autonomic nerve-supply.

The action of pilocarpine on the structures mentioned above is peripheral, being unaffected by section of the nerves, or by degeneration of the post-ganglionic fibres where this can be produced. For the latter observation the supply to the pupil from the oculomotor nerve affords the best subject of experiment. It has been shown by Anderson that section of the short ciliary nerves, or excision of the ciliary ganglion, with subsequent time for complete degeneration of the post-ganglionic fibres to the iris, increases rather than diminishes the effect of pilocarpine in producing constriction of the pupil. On the other hand atropine, which abolishes this effect of pilocarpine, leaves the fibres of the sphincter still responsive to direct electrical stimulation, or to the action of other peripherally acting drugs (*e. g.* ergotoxine). Pilocarpine, therefore, is said to act on the "nerve-endings" of the oculomotor nerve in the sphincter of the pupil, and the same conclusion applies by analogy to the other effects which we have hitherto described. Degeneration of the post-ganglionic sympathetic fibres to sweat-glands has likewise been found in animals to leave the action of pilocarpine on the glands intact.

While most of the marked actions of pilocarpine thus conform to a general scheme, having the relation described to the effects of autonomic nerves, there are certain of its effects which cannot be thus classified. We have noted already that the sympathetic nerve-endings in the sweat-glands react to pilocarpine like the cerebral autonomic endings in other gland cells. Then there is evidence that pilocarpine has, on the plain muscle of certain organs, a powerful stimulant action, which cannot be related to innervation from any source. Thus, its stimulant action on the uterine muscle of certain species, or on the retractor penis muscle, can only be attributed to direct action on the muscle fibres, though it is again abolished by atropine. Again, Cushny has pointed out that the uterus of the cat responds to the intravenous injection of pilocarpine as to stimulation of its purely sympathetic nerve supply or to the injection of adrenine. And there are other minor effects of pilocarpine which reproduce, somewhat weakly, effects of true sympathetic nerves. Thus, some vasoconstriction occurs, and becomes manifest in the small rise of blood pressure which is frequently seen when the cardiac inhibition, produced by a small dose of the alkaloid, passes off. The contraction of the spleen is a more marked effect which may be classed with this.

Even the effect on the eye is not wholly referable to the stimulation of cerebral autonomic endings, for, though the pupil is constricted, the nictitating membrane is withdrawn, as by sympathetic stimulation, when pilocarpine is given intravenously. Apart from the direct effect on plain muscle, already mentioned, two other types of action participate in producing these effects; and they are worthy of notice, in that they help to explain some of the features whereby the action in man differs from that to which animal experiments have given most prominence. Firstly, pilocarpine has, in addition to its peripheral action, a distinct, though relatively weak, action on ganglion cells. If a solution of the alkaloid is applied directly to the superior cervical ganglion of a cat, the immediate effect is a slight widening of the pupil and retraction of the nictitating membrane. As the alkaloid becomes absorbed into the blood stream and is carried to the eye, constriction of the pupil sets in. Since all the ganglion cells of the autonomic system appear to be pharmacologically equivalent, this ganglionic stimulation is probably a subsidiary factor even in such effects as the cardiac inhibition; though the theory formerly held, which attributed the whole effect on the heart to action on ganglion cells, is no longer tenable. Since the cells of the suprarenal medulla are morphologically homologous with sympathetic ganglion cells, it is not surprising to find evidence that they also are stimulated, by the injection of pilocarpine, to increased output of adrenalin into the circulation. This, again, will produce effects simulating sympathetic stimulation (see under *Adrenalin*).

In the effects of pilocarpine on plain involuntary muscle and gland cells we can recognise, therefore, in addition to its principal action referable to cranial and sacral autonomic nerve-endings, effects partly attributable to direct action on plain muscle, partly due to stimulation of ganglion cells, and partly secondary to accelerated output of adrenalin. With this experimental basis we may proceed to consider its general effects as exhibited in man and animals.

General Action.—In man the effects produced by injection or ingestion of a small dose of pilocarpine are salivation, sweating, flow of tears, and acceleration of pulse-rate, with a feeling of fullness in the head. This acceleration of the pulse-rate in man, by an alkaloid which characteristically inhibits the heart in animal experiments, has long been an anomaly and a puzzle. Recent observations suggest that it may be due to the demonstrated increase of adrenalin secretion. The same secondary effect may reasonably be held to play a part in the reputed beneficial effect of pilocarpine in asthma, which is in similar sharp contrast to the intense constriction of the bronchioles which it produces when injected intravenously into animals. With larger, poisonous doses vomiting is sometimes produced, and violent colicky pains in the intestines, with profuse watery evacuations, follow. The pupils become constricted, and the eyes accommodated for near vision by intense contraction of the ciliary muscle. These effects on the muscle of the eyeball may also be produced by instillation into the conjunctival sac. The stimulation of the endings of the oculomotor nerve is followed by partial paralysis, so that when the myosis passes off a slight mydriasis follows. The myosis is accompanied by a decrease in the intraocular tension.

Poisonous doses cause giddiness and confusion of ideas, muscular tremors and weak convulsions. The respiration becomes hurried and dyspnœic, and the excessive bronchial secretion causes rales to accompany the breath-sounds. Death, when it occurs, is said to be due to respiratory paralysis. In the case of the effect on sweat glands, clinical observation is curiously at variance with the indications of animal experiment as to the point of action. We saw above that the sweat glands of the cat still secrete in response to pilocarpine after degeneration of their nerve supply. In man, on the other hand, the effect is suppressed by interruption of the pre-ganglionic path. Thus if a cervical sympathetic nerve be divided by malignant growth, or other cause, pilocarpine fails to cause sweating on the corresponding half of the face. It is even stated that a break in conductivity of the spinal medulla causes failure of the sweating due to pilocarpine below the lesion. These differences are probably connected with differences in dose and in method of administration; but they also indicate that central effects are more, and peripheral effects less, prominent in man than in the lower animals, at any rate when the dosage of pilocarpine is within therapeutic limits.

The general effects seen in animal experiment may be deduced from the analytical account of the action given above, and may be summarised as follows.

Acceleration of all glandular secretions, except those which appear not to be under nervous control, viz. the bile, the milk, and the urine; contraction of the plain muscle of the eyeball, of the bronchioles, of the whole alimentary tract, the bladder, and the uterus; inhibition of the heart-beat, giving way, if the dose is large, to secondary paralysis of the vagus mechanism, with acceleration of the beat; certain secondary effects attributable to accelerated output of adrenalin, among which glycosuria may probably be included. The leucocytosis following an injection of pilocarpine is a lymphocytosis, according to Harvey, and attributable to contraction of the plain-muscle coats of spleen and lymph glands.

The antagonism between pilocarpine and atropine has already been mentioned. Of the two alkaloids atropine has by far the more powerful affinity for the tissues which both affect, so that the paralytic effect on any organ of even a minute dose of atropine can only be broken through by a dose of pilocarpine which is relatively very large.

Action of the other Alkaloids of Jaborandi.—These all exhibit, in varying degrees, an action of the pilocarpine type. Isopilocarpine is one-sixth to one-eighth as active as pilocarpine. It is probably a stereo-isomer of pilocarpine, differing in the configuration of the molecule with relation to one of the two asymmetric carbon atoms present. The relation between their activities is suggestively similar to that seen in the case of certain pairs of optical isomers. Pilocarpidine and pilosine are both much weaker. None of these exist in sufficient proportion to contribute significantly to the action of Jaborandi.

Therapeutics.—The principal use of Jaborandi and pilocarpine in therapeutics is the promotion of secretions, and particularly of sweating. It is undoubtedly the most powerful of the diaphoretics, but its use is limited by the depression following its action. In dropsy of renal origin it seems to have some value, but its most frequent use is in uræmia. As stated above it has no direct effect on renal secretion, and the relief of the plethoric circulation, by the large amount of water excreted in the sweat, is probably the main advantage to be obtained by its administration. The salts of pilocarpine are occasionally used, by local application, for producing myosis and relieving intraocular tension. The effect is less powerful and more evanescent than that of physostigmine.

Pilocarpine has sometimes been used, like physostigmine, for the relief of intestinal atony. Its use to promote uterine contraction has also been suggested. In either of these directions its possible value is discounted by its undesirable action on other tissues, and it has probably been finally displaced for such purposes by hypophyseal extract (see article on *Hormones*), which has not these disadvantages.

Preparations

Pilocarpinæ Nitras (B.P.).
Dose : $\frac{1}{20}-\frac{1}{5}$ gr. (3–12 mg.).
Injectio Pilocarpinæ Hypodermica (B.P.C.).
Dose : 2–8 min. (12–50 cl.). Strength 3 per cent.
Guttæ Pilocarpinæ (B.P.C.). 0·5 per cent.
Lamellæ Pilocarpinæ (B.P.C.). $\frac{1}{400}$ gr.
Pilocarpinæ Hydrochloridum (U.S.P.).
Dose : $\frac{1}{20}-\frac{1}{2}$ gr. (3–30 mg.).
Jaborandi Folia, Philocarpus (U.S.P.).
Extractum Jaborandi Liquidum (B.P. 1898).
Dose : 5–15 min. (3–10 dl.).
Tinctura Jaborandi (B.P. 1898). $\frac{1}{2}$–1 fl. dr. (2–4 ml.)
Fluidextractum Pilocarpi (U.S.P.). 30 min. (2 ml.).

The galenical preparations occurring in the British Pharmacopœia of 1898 are quite unnecessary. A salt of pilocarpine—preferably the nitrate, which is not hygroscopic—will serve every purpose for which Jaborandi used to be prescribed, and can be given in exact dosage.

Muscarine

This relatively simple alkaloid is not used in therapeutics, but it is toxicologically important and of great pharmacological interest. It was isolated by Schmiedeberg from the fly agaric, Amanita muscaria, a fungus which has been responsible for many cases of mushroom-poisoning. The proportion of muscarine present in this mushroom varies very greatly, and some at least of the poisonous properties must be due to other, unidentified constituents. A substance identical with, or closely related to muscarine, has been obtained from putrefied proteins, and it seems not impossible that the presence of muscarine in Amanita muscaria may be due to secondary putrefactive or fermentative changes, to which the tissues of fungi are conspicuously liable.

Muscarine always occurs closely associated with choline, to which it is beyond doubt related chemically, though the exact nature of the relation is still in doubt. The empirical formula suggests that it is an oxidation-product of choline, and by treatment with nitric acid it is possible to prepare from choline a substance which is chemically very similar to the natural muscarine. But this synthetic "muscarine" has only about one-tenth of the characteristic activity of the natural base, and exhibits, in addition, a curare-like activity, which the natural base does not possess. The most recent observations indicate that the synthetic muscarine is a nitrous ester of choline.

Action.—The action of muscarine very closely resembles that of pilocarpine; but the effects on involuntary muscle are relatively rather more prominent, those on secretory glands rather less prominent in the action of muscarine than in that of pilocarpine. The most characteristic and conspicuous of its actions is inhibition of the heart by stimulation of vagus nerve-endings. This effect is produced on the frog's heart by muscarine in very high dilutions, and the heart of the cat is relatively even more sensitive to its action. Other effects, likewise attributable to stimulation of cerebral and sacral autonomic nerve-endings, are constriction of the pupil and

spasm of accommodation, bronchial spasm, and violent peristalsis of the stomach and intestines.

The effects of muscarine, like those of pilocarpine, are all annulled by relatively small doses of atropine and its allies.

Arecoline

This is the active alkaloid of the areca or betel-nut. Its action is again closely similar to that of pilocarpine. It is not used in human therapeutics, but has been employed in veterinary medicine.

Calabar Bean and Physostigmine

Calabar beans are the ripe seeds of a climbing plant, *physostigma venenosa*, which grows in West Africa. They came to notice through their use by the natives as an "ordeal poison." Their action is that of the principal alkaloid, physostigmine or eserine; another alkaloid, eseridine, has apparently a similar but weaker action. Little is yet known as to the structure of these alkaloids.

Action of Physostigmine.—In its peripheral effects on involuntary muscle and glands, the action of physostigmine is broadly similar to that of pilocarpine and muscarine, though it differs with regard to the relative intensity of the effects on the different organs concerned. Its constricting action on the pupil is very intense, and very readily produced by local application to the conjunctiva. Anderson has shown this action depends on the integrity of the post-ganglionic fibres from the ciliary muscle, disappearing when these degenerate, but reappearing with their regeneration before electrical excitability is regained. Physostigmine has a similar action on the ciliary muscle, producing powerful spasm of accommodation. From a practical point of view, however, its most important action on the eye is probably the fall of intraocular tension which it causes, especially when this is abnormally high. It is believed that this effect is, in the main, secondary to its action on the pupil and the ciliary muscle, the constricted condition facilitating the escape of aqueous humour through the sinus venosus scleræ (canal of Schlemm). Diminution of the rate of formation of the aqueous humour, by arterial constriction, may also play some part in the action. Physostigmine causes inhibitory slowing of the heart after section of the vagi, but far less powerfully than muscarine or pilocarpine; indeed, the inhibitor effect of a small dose is frequently latent, being only demonstrable as an increased liability of the heart to inhibition when the vagus is stimulated. This inhibitory action, referable to the vagus nerve-endings, appears to be complicated, moreover, by a direct excitatory action on the heart muscle, comparable with the direct action on plain muscle to which reference is made below. This probably explains the fact that, though physostigmine will produce inhibitory slowing, when applied to the normal frog's heart, it will release the same heart from a complete standstill produced by muscarine.

Physostigmine stimulates secretion of saliva and sweat, even when the secretory nerves have been cut; but the action in this direction is, again, less powerful than that of pilocarpine, and may be manifested chiefly as an increase in the responsiveness of the submaxillary gland, for example, to electrical excitation of the chorda tympani. It has been suggested, indeed, by Loewi and Mansfeld, that the action of physostigmine differs from that of pilocarpine and muscarine, in that the former does not, of itself, act as a stimulus, but merely raises the excitability of the peripheral organs to impulses in cerebral autonomic nerves. The difference between the action of these alkaloids seems adequately accounted for, however, by stating that the effect of physostigmine on certain organs, such as the heart or salivary glands, is weaker, and, when the dosage is small, may be subliminal.

Physostigmine has a pronounced stimulant action on the muscular walls of the stomach, intestines and urinary bladder, and vomiting and purging are prominent symptoms of its action on the intact animal. It produces also intense constriction of the bronchioles.

These various actions may be summarised, like the corresponding effects of pilocarpine and muscarine, as a stimulation of the endings of cerebral and sacral autonomic nerves. It would appear, indeed, from the experiments of Anderson mentioned above, that the action of physostigmine may be located at autonomic nerve-endings in a more truly morphological sense, as structures in trophic continuity with the post-ganglionic fibres. It should be noted also that the most prominent features in this physostigmine action are stimulant effects on involuntary muscle, whereas with pilocarpine the effect on secreting glands is more emphasised. Physostigmine, like pilocarpine, has also a direct stimulant effect on plain muscle, such as that of the uterus, which has no cerebral or sacral autonomic nerve-supply. The fact that it produces a rise of blood pressure, due to vaso-constriction, when given in doses not so large as to cause severe cardiac inhibition, is possibly another example of this action on all plain muscle; but the phenomenon needs further investigation.

These various effects of physostigmine on involuntary muscle and gland cells are antagonised by atropine. Atropine is the more powerful of the antagonists, but its action is not so overwhelmingly potent against physostigmine

as against pilocarpine or muscarine; so that it is comparatively easy to weaken or remove an atropine paralysis by a larger dose of physostigmine. The latter can, therefore, be effectively employed to accelerate the return of normal function after paralysis of the pupil and ciliary muscle by atropine in ophthalmic work. It is a little difficult to reconcile this antagonism to atropine with the disappearance of physostigmine action after degeneration of post-ganglionic autonomic fibres; for atropine (q.v.) also paralyses the effects of pilocarpine and muscarine, which are independent of the integrity of these fibres.

There is evidence that physostigmine, like pilocarpine, accelerates the output of adrenalin from the suprarenal glands (Tscheboksaroff), but the extent to which this effect may complicate the action has not yet been investigated.

Physostigmine has a curious and characteristic action on striped muscle, which is thrown into a persistent tremulous twitching. The muscles of the hind-limbs are first affected, and the action progresses till the whole voluntary musculature is involved. This effect is particularly prominent in mammalia. It is peripheral in origin, being unaffected by section of motor nerves, but antagonised by curare. It is stated that the action disappears when the motor nerves are allowed to degenerate—a fact which would appear to locate the action at the terminal arborisations of their fibres. But, on the other hand, the paralysis of motor nerves by curare can be broken through by larger doses of physostigmine, so that the action of these larger doses, at any rate, must be held to extend to more peripheral structures. The difficulty is similar to that mentioned above in connection with the antagonism to atropine.

Physostigmine has in all animals a depressant effect on the central nervous system. In the frog it is stated that the higher centres are first affected, so that voluntary movement is lost before respiration ceases, and spinal reflexes survive still longer. In mammals, on the other hand, and especially in man, there is evidence that the spinal medulla and bulbar centres are affected before consciousness is impaired. In the cat, and possibly in man, the depression is preceded by a period of excitation.

Symptoms of Poisoning.—Poisoning by calabar bean or physostigmine is attended by symptoms which can readily be deduced from the foregoing account of the action—severe abdominal pain, vomiting, purging, dyspnœa, muscular weakness and tremor, pin-point pupils, sweating, salivation, slow heart-beat, and dyspnœa. It is not clear to what extent the dyspnœa is referable to a preliminary rise in excitability of the bulbar centres, and to what extent, on the other hand, it can be explained by the asthma-like spasm of bronchiolar musculature. Death, when it occurs, is due to respiratory paralysis. The stomach should be washed out if the poison has been swallowed, atropine injected, and artificial respiration applied when necessary.

Therapeutics.—Physostigmine has been tried as a hypodermic purgative, but its action is attended with painful griping and complicated by vomiting, so that it has no real value in this direction. It was, however, until recently practically the only drug available in post-operative paralytic distension of the bowel, though its efficacy does not seem to have been great. It is probable that it has now been permanently displaced for this purpose by the use of hypophyseal (infundibular) extract. In veterinary practice, however, it still finds use in treating certain forms of paralytic obstruction.

As a diaphoretic it is inferior to pilocarpine, and it may be stated that the only real value of physostigmine in human practice lies in its effect on the eyeball when applied locally. It is used not uncommonly to accelerate the return of normal control over pupil and accommodation after atropinisation, but its greatest value lies in its power of reducing intraocular tension, for which it is used in glaucoma. For instillation the salts are dissolved in water in 0·25 to 1 per cent. solution. The addition of a small proportion of boric acid renders the solution more stable. The salts may also be applied in the form of lamellæ. Many practitioners prefer for instillation a solution of the free alkaloid in oil, which is more stable and less irritant than aqueous solutions of the salts.

Preparations

Physostigminæ Sulphas (B.P., U.S.P.)
Dose: $\frac{1}{64}$–$\frac{1}{32}$ gr. (1–2 mg.).
Lamellæ Physostigminæ (B.P.)
$\frac{1}{1000}$ gr. (0·065 mg.) in each.
Guttæ Physostigminæ (B.P.C.). 1 per cent.
Guttæ Physostigminæ et Cocaine (B.P.C.). 0·25 per cent. with 1 per cent. Cocaine Hydrochloride.
Oculentum Physostigminæ (B.P.C.). 0·2 per cent. with Soft Paraffin (white).
Physostigminæ Salicylas. (U.S.P.)
Dose: $\frac{1}{60}$–$\frac{1}{20}$ gr. (1–3 mg.).
Physostigmatis Semina, Physostigma (U.S.P.).
Extractum Physostigmatis (U.S.P.). 2 per cent. of alkaloids.
Average Dose: $\frac{1}{8}$ gr. (8 mg.).
Tinctura Physostigmatis (U.S.P.). 0·014 per cent. of alkaloids.
Average Dose: 15 min. (1 ml.).

The alkaloid and its salts fulfil all the requirements of rational employment of the drug,

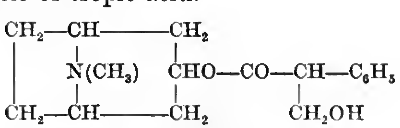
and the galenical preparations have now been dropped from the British Pharmacopœia (1914).

Belladonna, Hyoscyamus and Stramonium
[containing the alkaloids of the Atropine series]

Among a number of plants belonging to the Solanaceæ, which contain alkaloids belonging to this series, are the three mentioned above. Of Atropa Belladonna (Deadly Night-shade) the leaves and root, of Hyoscyamus Niger (Henbane) the leaves, of Datura Stramonium (Thorn-apple) the leaves and seeds, and of Scopola carniolica the dried rhizome, are usually employed for the preparation of drugs.

The use of synonyms has confused the nomenclature of the alkaloids in these drugs, and has given the subject a fictitious complexity. The conception is considerably simplified by stating that only two alkaloids of importance occur in the official members of the series, but that each of these is optically active, and can, therefore, exist in lævorotary, dextrorotary or racemic form. The lævorotary and racemic forms are found in the extracts and preparations in varying proportions, the dextrorotary forms only being obtainable by special methods of separation from the racemic. It is not improbable that the plants contain the lævorotary forms only, these becoming racemised to varying degrees in the process of extraction. One of these alkaloids is known in its lævorotary form as *hyoscyamine*, in its racemic form as *atropine*. The other is known as *hyoscine* or *scopolamine*, and the name *atroscine* has been suggested for its racemic form, but has not obtained any wide currency. Hyoscine, indeed, contains two asymmetric carbon atoms, so that four different optical isomers are possible. The hyoscine usually obtained is lævorotary in varying degrees, and may be regarded as a mixture of racemic and lævorotary varieties of the alkaloid.

Atropine (or hyoscyamine) consists of a basic nucleus called *tropine*, which is closely related to the ecgonine nucleus of cocaine, united to a radicle of tropic acid.



Tropine nucleus Tropyl radicle.

By substituting other acids a series of artificial "tropeines" has been obtained, of which one, containing the mandelic acid radicle, is known as *homatropine* and has considerable practical value. The basic nucleus in hyoscine (or scopolamine) is different from, though closely related to tropine, and is known as *oscine* or *scopoline:* this is again combined with a tropic acid radicle.

Belladonna leaves contain hyoscyamine, and the root is said to contain some hyoscine also. The other official members of the series contain hyoscyamine and hyoscine in varying proportions, hyoscine being the predominant alkaloid in scopola. Racemisation occurs to varying degrees in the process of extraction, so that the extracts and preparations are described as containing hyoscyamine, atropine and hyoscine in different proportions.

Action.—These alkaloids exhibit a twofold action; they paralyse certain autonomic nerve-endings, and they have an action on the central nervous system. The two types of action may be considered separately.

Peripheral Action.—This is qualitatively similar in the different alkaloids, and may be described for atropine, as the most familiar member of the series. The peripheral action of atropine is most easily considered with reference to those of pilocarpine, muscarine and physostigmine. It exhibits a very exact physiological antagonism to these alkaloids, paralysing with great precision all those effects on involuntary muscle and gland cells which their stimulant action produces, and no others. A reference to the section dealing with either pilocarpine or physostigmine will show that such antagonism involves a paralytic action by atropine on the nerve-endings of the cerebral and sacral autonomic systems and of the true sympathetic nerve-endings in the sweat glands. On the whole this is a true summary of the peripheral action of atropine, but it needs some qualification. In many cases, as we shall see, atropine not only annuls the peripheral effect of pilocarpine or physostigmine, but blocks the passage of impulses from the autonomic nerves, which normally produce the corresponding effects. In other cases, however, while the obliteration of the action of pilocarpine is complete, the corresponding effect produced by electrical stimulation of the autonomic nerve-supply is practically unaffected by atropine in ordinary doses. In such cases the term "autonomic nerve-ending," to describe the site of the reciprocal effects of pilocarpine and atropine, becomes peculiarly inappropriate.

Taking the peripheral actions of atropine in detail, we find that it diminishes secretions in general, and entirely arrests most when given in adequate doses. Those which escape suppression are those which are not at all, or only in part, under nervous control. Thus the secretion of bile and of milk are said to be somewhat diminished; the effect of the vagus and of pilocarpine on pancreatic secretion are abolished, but the secretion of the juice in response to secretin is not perceptibly affected. The secretion of gastric juice is also depressed by atropine, which is said to diminish the

hydrochloric acid disproportionately to the other constituents. The secretion of urine and lymph are not diminished. Atropine readily abolishes the secretion of saliva, of tears, and of the lubricant mucus of the mouth, pharynx, respiratory passages and œsophagus. If the flow of saliva from the submaxillary duct is observed in an anæsthetised animal, it is found that very small doses of atropine or its allies abolish the secretion produced by stimulation of the chorda tympani or injection of pilocarpine. Secretion can still be produced at this stage by stimulating the cervical sympathetic nerve or injecting adrenine intravenously, and much larger doses of atropine are needed to depress or abolish the effect of stimulating the sympathetic nerve supply to the gland by either method. The sympathetic nerve-endings in the sweat glands, on the other hand, are as sensitive to the paralysing action of the atropine series as they are to the stimulant action of pilocarpine, showing, in both respects, a pharmacotropic affinity with the cerebral autonomic rather than with the true sympathetic system, to which latter they morphologically belong.

Atropine readily paralyses the effect of the oculomotor nerve on the sphincter of the pupil and the ciliary muscle, so that a marked feature of its action is mydriasis and loss of power of accommodation. Probably as a result of this action, it causes a considerable rise of intraocular tension, being in this respect, again, a perfect antagonist of physostigmine. The action on the pupil serves particularly well for the more exact localisation of the effect. Degeneration experiments show that the action must be located at the same level as that of pilocarpine (q.v.)—*i. e.* on some structure associated with innervation by the autonomic fibres, and on the path of impulses passing from them to the muscle, but trophically independent of them. These effects of atropine on the eye are readily produced by local application.

Atropine in very small doses annuls the inhibitor effect of the vagus on the heart, and the motor action of the same nerve on the muscular coats of the bronchioles, as well as the corresponding effects of pilocarpine, muscarine and physostigmine. Its action on the œsophagus exhibits an instructive variation, in accordance with the formation of the muscular coats of that tube from striated or non-striated muscle. Only in the latter case is the control by the vagus paralysed by atropine. In some animals, such as the cat, the upper part of the œsophagus has striated, the lower part unstriated, muscle. The control of the former by the vagus is unaffected by atropine, but paralysed by curare, while the reverse is true of the latter. Similarly, the sphincter of the pupil in birds consists of striated muscle fibres, and its control by the oculomotor nerve is unaffected by atropine, but paralysed by curare.

It has been stated that atropine has a direct stimulant action on the heart, and an attempt has even been made to explain the paralysis of the heart vagus as due simply to increased excitability of the muscle. (Fröhlich and Lœwi.) But there is little evidence of the effect, and still less ground for its use to explain away one of the most characteristic of the paralytic actions of atropine.

On the endings of cerebral and sacral autonomic nerves in other tracts of involuntary muscle atropine has far less effect. Thus it leaves the vasodilator actions of the chorda tympani and the nervi erigentes unaffected, when given in doses which annul the secretomotor effect of the former. The motor effects of the vagi and pelvic nerves on the muscular coats of the stomach, intestines and urinary bladder are similarly resistant to its paralytic action, only showing a partial depression even with large doses. These exceptions are the more striking, in that it very readily abolishes the corresponding effects of pilocarpine and physostigmine. The effects produced by nerves of the true sympathetic system, whether motor or inhibitor, are also relatively immune to the action of atropine, with the exception of the secretion of sweat, the abnormal position of which has been already discussed. The corresponding effects of adrenine are likewise not materially modified by small doses of atropine.

In addition to these highly specific actions, atropine in larger doses has a depressant action on all involuntary muscle, though in the whole animal this is largely masked by the central effects, which will be considered later. The fact that atropine causes a vaso-dilator fall of blood pressure in an animal with the medulla oblongata destroyed, while a rise of blood pressure, in which splanchnic vaso-constriction plays some part, follows its injection in the animal with intact nervous system, seems to indicate an antagonism between stimulation of the medullary vasomotor centre and peripheral depression of plain-muscle tone. A similar antagonism may possibly explain the discrepancy between the depression of spontaneous movements in stomach and intestine, seen in experiment, on the one hand, and the vomiting and purging produced in some cases by poisonous doses of atropine in man, on the other.

In producing all the peripheral effects on involuntary muscle and gland cells hyoscyamine (lævorotary) is practically twice as active as the racemic atropine; the dextrorotary isomer having, as Cushny has shown, only a small fraction of the activity of the lævorotatory. There still exists some doubt as to the relation of the activity of hyoscine on the peripheral

endings to that of atropine, probably owing to the use, by different observers, of preparations containing the different isomers in varying proportions. The general opinion is that hyoscine, as a local mydriatic, is more powerful, more rapid, but more evanescent in action than atropine. Cushny and Peebles found l.-hyoscine twice as active as r.-hyoscine in paralysing salivary secretion and vagus inhibition of the heart.

Homatropine is much weaker and much less toxic than atropine, and its effect on the pupil is more rapid and very much more evanescent. It is, therefore, widely used in ophthalmic work, especially when mydriasis only, without complete paralysis of accommodation, is required. The action of the quarternary methobromide of homatropine is said to be even more evanescent than that of the ordinary salts.

Certain other peripheral effects should also be mentioned, which are best known as effects of belladonna, and are, therefore, usually attributed to atropine; the relative efficacy of the different alkaloids in producing them not having been studied. Such are the local anæsthetic effect, due to paralysis of sensory nerve terminations, on account of which plasters and liniments containing belladonna are applied in relieving pain. The flushing of the skin vessels, especially over the "blushing" area, may also be mentioned here, though there is evidence that it is central in origin. In sensitive individuals taking belladonna, an eruption frequently develops over this area, very similar to that of scarlatina.

Effects on the Central Nervous System.—In the frog a double action of atropine on the central nervous system is very obvious. After a brief stage of excitement a marked depression ensues and the frog lies quite motionless, exhibiting no respiratory movements or reflex action. After a variable interval, usually twenty-four hours or more, a condition of pronounced reflex excitability appears, practically identical with that produced by strychnine. An interesting light has been thrown on this double action by the work of Cushny, who showed that l.-hyoscyamine is predominantly depressant, d.-hyoscyamine predominantly excitatory on the frog's central nervous system; so that the racemic atropine shows in succession the action of each constituent isomer. Both isomers produce, in the frog, a weak curare-like action also, which somewhat moderates the strychnine-like effect. In the mammal there is no such marked contrast, both lævo-hyoscyamine and atropine producing an excitatory action on the brain and medulla oblongata, which is succeeded by depression with large doses, death being caused by paralysis of the respiratory centre. In man the cerebral symptoms produced by atropine are garrulity, confusion of ideas, emotional instability, passing into delirium, which may be maniacal in its violence. The effect is superficially similar to that of alcohol, but appears to be due to direct excitation rather than to weakening of inhibitor control. Muscular tremor and convulsions are seen after large doses, and are succeeded by sleep, deepening into coma. The body temperature is usually raised. The respiration is stimulated by therapeutic doses, but becomes weakened in the depressant phase of the action of large doses, its failure being the cause of death in fatal poisoning. The effect on the vasomotor centre has already been mentioned. In man l.-hyoscyamine exhibits a difference in action from atropine of the same kind as, though less marked and uniform than that seen in the frog. Both atropine and hyoscyamine may produce sleep without the preliminary stage of excitation, and this is much commoner with hyoscyamine than atropine. It is to be expected, therefore, that d.-hyoscyamine would exhibit a more violent and uniform excitatory action, but there is no record of the action of the pure d.-base on the human subject.

In the case of hyoscine the narcotic effect becomes the predominant feature of the central action even with very small doses, though traces of an initial stimulant action can sometimes be detected. The sleep which it produces is said to resemble natural sleep more nearly than that induced by opium. According to Cushny and Peebles no difference in hypnotic power could be detected between l.-hyoscine and r.-hyoscine in a series of observations on man.

Symptoms of Poisoning.—In poisoning by belladonna a combination of the peripheral and central effects of atropine is seen—dry mouth and skin, difficulty in swallowing, husky phonation, dilated pupils, indistinct vision, and rapid heart-beat being associated with accelerated respiration and the symptoms of cerebral excitation mentioned above. When large doses have been taken the symptoms of depression appear later, the patient lapsing into stupor, the heart becoming slow and feeble from direct action on its muscle, and the respiration gradually failing. Hyoscine, though active in very small doses, is much less dangerous than atropine in excessive doses. It is usually narcotic in action from the first, and though the peripheral action corresponds, on the whole, to that of atropine, the acceleration of the heart is much less marked.

Therapeutic Uses.—Various preparations of belladonna are used externally for their anodyne effect, though the rationale of their use in this manner is not, in all cases, obvious. For effects depending on paralysis of autonomic terminations atropine is the most generally used alkaloid of the series. Thus it is given to control

excessive sweating, especially the night-sweats of phthisis, and belladonna is often applied as a plaster to the breasts, when it is desirable to check the secretion of milk, though probably the effect of such a plaster is largely mechanical. Atropine, again, is a common constituent of preparations applied as a spray to the respiratory passages in asthma, its effect being partly due to relaxation of bronchial spasm, partly to checking of bronchial secretion. Stramonium is also commonly employed in asthma, the inhaling of the smoke of cigarettes prepared from the leaves being a favourite method of application. The use of belladonna internally in whooping cough probably depends chiefly on the reduction of secretion.

The value of atropine or belladonna in controlling intestinal spasm is not easily understood. Possibly it weakens the effect of the vagus on intestinal muscle, or diminishes the local reflexes, to a greater extent in man than in the animals which have formed the subjects of experimental investigation. That it diminishes painful, irregular, local contractions of the bowel, without producing constipation, seems beyond doubt. Atropine, hyoscyamine, or the extracts of belladonna or hyoscyamus, are frequently given for this reason with the more drastic purgatives, to reduce painful griping, and the extracts are said to have great value in removing intestinal stasis, and restoring normal activity to an atonic colon. Atropine and belladonna are also given to allay painful spasms of other organs, such as those due to calculi in the biliary or urinary passages. The well-recognised value of belladonna in enuresis may be an effect of the same kind, the excessive responsiveness of the bladder to mild distension being allayed.

For its paralytic effect on the heart vagus, atropine is sometimes given before chloroform and other general anæsthetics, to check the tendency to excessive cardiac inhibition. But the chief practical application of its peripheral paralysis of autonomic endings is its use in dilating the pupil and paralysing accommodation in ophthalmic surgery. For dilatation as a preliminary to retinoscopy homatropine is often substituted, but when the accommodation is to be paralysed atropine is much more certain in action. Atropine is also used for breaking down adhesions of the iris to the lens, and for relieving the painful reflex ciliary spasm produced by corneal injuries and ulcers. The rise of intraocular tension which they produce makes all the alkaloids of the series dangerous when there is any suspicion of glaucoma. The latter condition sometimes appears as a sequel to the diagnostic use of atropine, and many surgeons give a precautionary instillation of physostigmine when examination under atropine has been completed.

Atropine and the other members of the series are always applied locally when their effects on the eye are required. Solutions of the salts in water, or of the bases in oil or ointments, are introduced into the conjunctival sac; or small discs containing the salts may be placed on the conjunctiva and allowed to dissolve.

The only important use of atropine for its central effects depends on its stimulation of the medullary centres. It is used to counteract the respiratory depression in narcotic, and especially in morphine poisoning, and is very generally prescribed with morphine for the same reason. Hyoscine, on the other hand, is prescribed for its central action almost exclusively. It finds extensive use as an hypnotic, especially for insane patients, or where morphine is considered inadvisable, as in renal disease. Recently the use of a combined injection of hyoscine (scopolamine) and morphine, as a preliminary to general anæsthesia by chloroform or ether, or to dull sensation during labour, has acquired considerable vogue, especially on the continent of Europe.

Preparations

Belladonnæ Folia (B.P., U.S.P.).
- Extractum Belladonnæ Siccum (B.P.). 1 per cent. of alkaloids.
  Dose: $\frac{1}{4}$–1 gr. (16–60 mg.).
- Tinctura Belladonnæ (B.P.). 0·035 per cent. of alkaloids.
  Dose: 5–15 min. (3–10 dl.).
- Extractum Belladonnæ Foliorum (U.S.P.). 1·4 per cent. of alkaloids.
  Average Dose.: $\frac{1}{5}$ gr. (10 mg.).
- Tinctura Belladonnæ Foliorum (U.S.P.). 0·03 per cent. of alkaloids.
  Average Dose: 8 min. (5 dl.).
- Emplastrum Belladonnæ (U.S.P.). 0·4 per cent. of alkaloids.
- Unguentum Belladonnæ (U.S.P.).
- Extractum Belladonnæ Viride (B.P., 1898). $\frac{1}{4}$–1 gr. (15–60 mg.).
- Succus Belladonnæ (B.P., 1898). 5–15 gr. (3–10 dl.).

Belladonnæ Radix (B.P., U.S.P.)
- Extractum Belladonnæ Liquidum (B.P.). 0·75 per cent. of alkaloids.
- Suppositoria Belladonnæ (B.P.). 1 mg. of alkaloids in each.
- Emplastrum Belladonnæ (B.P.). 0·25 per cent. of alkaloids.
- Linimentum Belladonnæ (B.P.). 0·375 per cent. of alkaloids.
- Unguentum Belladonnæ (B.P.). 0·6 per cent. of alkaloids.
- Fluidextractum Belladonnæ Radicis (U.S.P.). 0·4 per cent. of alkaloids.
  Average Dose: 1 min. (5 cl.).

Linimentum Belladonnæ (U.S.P.).
Extractum Belladonnæ Alcoholicum (B.P., 1898.).
Dose: $\frac{1}{4}$–1 gr. (15–60 mg.).

Hyoscyami Folia (B.P., U.S.P.).
Extractum Hyoscyami (B.P., U.S.P.). 0·3 per cent. of alkaloids.
Dose: 2–8 gr. (12–50 cg.).
Tinctura Hyoscyami (B.P., U.S.P.). 0·007 per cent. of alkaloids.
Dose: $\frac{1}{2}$–1 fl. dr. (2–4 ml.).
Fluidextractum Hyoscyami (U.S.P.). 0·075 per cent. of alkaloids.
Average Dose: 3 min. (2 dl.).
Extractum Hyoscyami Viride (B.P., 1898.). 2–8 gr. (12–50 cg.).
Succus Hyoscyami (B.P., 1898). $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

Stramonii Folia (B.P., U.S.P.).
Tinctura Stramonii (B.P.), (U.S.P.). 0·025 per cent. of alkaloids.
Dose: 5–15 min. (3–10 dl.)
Extractum Stramonii (U.S.P.). 1 per cent. of alkaloids.
Average Dose: $\frac{1}{5}$ gr. (10 mg.).
Fluidextractum Stramonii (U.S.P.). 0·25 per cent. of alkaloids.
Average Dose: 1 min. (5 cl.).
Pulvis Stramonii Compositus (B.P.C.).

Stramonii Semina (B.P., 1898).
Extractum Stramonii (B.P., 1898).
Dose: $\frac{1}{4}$–1 gr. (16–20 mg.).

Scopola (U.S.P.).
Extractum Scopolæ (U.S.P.). 2 per cent. of alkaloids.
Average Dose: $\frac{1}{5}$ gr. (10 mg.).
Fluidextractum Scopolæ (U.S.P.). 0·5 per cent. of alkaloids.
Average Dose: 1 min. (5 cl.).

Atropina (B.P., U.S.P.).
Dose: $\frac{1}{200}-\frac{1}{100}$ gr. (0·3–0·6 mg.).
Unguentum Atropinæ (B.P.). 2 per cent.

Atropinæ Sulphas (B.P., U.S.P.).
Dose: $\frac{1}{200}-\frac{1}{100}$ gr. (0·3–0·6 mg.)
Liquor Atropinæ Sulphatis (B.P.). 1 per cent.
Dose: $\frac{1}{2}$–1 min. (3–6 cl.).
Lamellæ Atropinæ (B.P.). $\frac{1}{5000}$ gr. (0·013 mg.). Atropine Sulphate in each.
Hyoscyaminæ Sulphas (B.P., U.S.P.).
Dose: $\frac{1}{200}-\frac{1}{100}$ gr. (0·3–0·6 mg.).
Hyoscyaminæ Hydrobromidum (U.S.P.).
Dose: $\frac{1}{200}-\frac{1}{100}$ gr. (0·3–0·6 mg.).
Hyoscinæ Hydrobromidum (B.P., U.S.P.)
Dose: $\frac{1}{200}-\frac{1}{100}$ gr. (0·3–0·6 mg.).
Homatropinæ Hydrobromidum. (B.P., U.S.P.).
Dose: $\frac{1}{64}-\frac{1}{32}$ gr. (1–2 mg.).
Lamellæ Homatropinæ (B.P.).
Dose: $\frac{1}{100}$ gr. (0·65 mg.) in each.

Colchicum and Colchicine

Colchicine is the principal alkaloid contained in the corm and seeds of colchicum autumnale, the meadow saffron. It had been included in this group on account of certain actions on plain muscle, which are paralysed by atropine, and are regarded by Dixon and Malden, who described them, as analogous to those of pilocarpine, muscarine and physostigmine. It is a feeble, amorphous base, of unknown constitution, dissolving in water to form a solution neutral to litmus. It is readily oxidised to form oxydicolchicine.

Action.—When it is injected into the circulation, the immediate effects of colchicine are comparatively slight. The blood pressure falls, on account of some weakening of the heart's action, and the plain muscle of various organs—the intestine, spleen, uterus and bronchi—is stimulated to contraction. These effects are prevented or abolished by atropine, and are in that respect similar to those of pilocarpine or physostigmine. The glands are not excited to secretion, however, and the heart is not inhibited to any marked extent.

These immediate effects soon pass off, and the animal remains normal for several hours. Then a secondary train of symptoms appears, the animal showing signs of central depression. With the onset of these secondary symptoms, the blood pressure begins to fall, and when the animal dies of respiratory failure, after a period of unconsciousness, the splanchnic area is found to be engorged with blood. The respiration is rendered slower and deeper at first, but later becomes continually shallower, till it finally ceases. Post-mortem a varying degree of inflammatory congestion is seen in the mucous membrane of the intestine. Symptoms of renal irritation are seen during life, the urine being often bloody, and sometimes suppressed. Dixon and Malden showed that colchicine produced an initial leucopenia, followed by a more marked leucocytosis, which appeared to be due to a stimulation of the hæmopoietic function of the bone marrow. Colchicine has an intense local irritant action on all mucous membranes.

These delayed effects, which form the most prominent feature of the action of colchicine, dissociate it from the rest of the group in which it is here included. In some respects they show similarity to the action of various protein poisons. The symptoms of colchicine poisoning are very similar to those of some cases of "ptomaine poisoning," for example, or to those produced by the poisonous proteins obtained from sea-anemones and mussels and investigated by Richet. This again associates colchicine with the class of so-called blood-capillary poisons, to which a number of metals, as well as protein poisons, belong.

As in all these cases, there is some difficulty in deciding how much of the central depression is due to direct action of the poison on the brain and spinal medulla, how much is secondary to the inflammatory changes produced during its excretion by the bowel and the kidney.

According to Jacobi colchicine is oxidised in the mammalian circulation to oxydicolchicine, which produces similar effects when injected. In the frog this oxidation does not occur, and colchicine is without action. If the colchicine is oxidised to oxydicolchicine before injection, however, the latter produces in the frog a veratrine-like effect on muscle and a strychnine-like effect on the cord. The latter action strongly favours the view that the central effects in the mammal are, at least in large part, due to direct action.

In man poisonous doses of colchicine produce abdominal pain, salivation, vomiting, diarrhœa and collapse. The evacuations sometimes continue till only bloody mucus is passed. Paralytic symptoms begin with the lower extremities, and the paralysis ascends till respiration is involved and death ensues.

Therapeutics.—Colchicum and colchicine are used only in gout, in which their beneficial effect is attested by clinical experience, but has no rational basis as yet. In therapeutic doses they produce none of the above toxic symptoms, but purging may result if the administration is pushed. The leucocytosis may be concerned in the beneficial effects, but it is not clear how.

Materia Medica and Preparations

Colchici Cormus (B.P., U.S.P.).
  Extractum Colchici (B.P.).
    Dose : $\frac{1}{4}$–1 gr. (16–60 mg.).
  Vinum Colchici (B.P.).
    Dose : 10–30 min. (6–18 dl.).
  Extractum Colchici Cormi (U.S.P.). 1·4 per cent. Colchicine.
    Average Dose : 1 gr. (6 cg.).
Colchici Semina (B.P., U.S.P.).
  Tinctura Colchici (B.P.).
    Dose : 5–15 min. (3–10 dl.).
  Fluidextractum Colchici Seminis. (U.S.P.). 0·5 per cent. Colchicine.
    Average Dose : 3 min. (2 dl.).
  Tinctura Colchici Seminis (U.S.P.). 0·04 per cent. Colchicine.
    Average Dose : 30 min. (2 ml.).
  Vinum Colchici Seminis (U.S.P.).
    Average Dose : 30 min. (2 ml.).
Colchicina (U.S.P.).
  Dose : $\frac{1}{120}-\frac{1}{30}$ gr. (0·5–2 mg.).

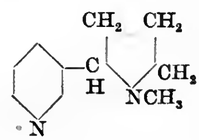
The Vinum Colchici is the preparation usually prescribed. H. H. D.

DRUGS ACTING ON THE AUTONOMIC GANGLION CELLS AND ON MOTOR END-PLATES

In the brief outline of the autonomic system given on p. 622 it was mentioned that the nerve-cells of this system, to whichever of its primary divisions they belong, show a pharmacological uniformity, so that an alkaloid which stimulates or paralyses one, has this effect on all. It must now be added that the motor end-plates of voluntary muscle-fibres, on which the cerebro-spinal motor nerve-fibres end, show similar pharmacological affinities. We have, then, a fairly well-defined group of alkaloids, which exhibit a stimulant or paralytic action, and in many cases both in succession, on autonomic ganglion cells and the motor end-plates of skeletal muscle. There are considerable differences in the activity, some being powerfully stimulant, others predominantly paralytic in action; some acting more on ganglion cells, others affecting the end-plates preferentially. All have, in addition, some action on the central nervous system. None have great therapeutic importance.

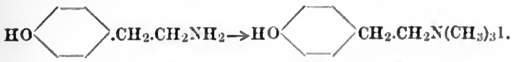
Nicotine, Lobeline, Cytisine

These alkaloids may be treated together, as their action is so closely similar that very special precautions would be necessary to differentiate them by pharmacological experiment. Nicotine is the active alkaloid of tobacco, which is not now used in therapeutics. It is constructed of a pyridine and a methyl-pyrollidine nucleus—



The alkaloid of Duboisia Hopwoodii, the leaves of which are chewed by the Australian natives, was formerly called Piturine, but is now known to be identical with nicotine. Nicotine as a free base forms an oily, volatile liquid, with a strong alkaline reaction in watery solution. The salts can be crystallised. Lobelia inflata, smoked by some of the North American native tribes, and therefore known as "Indian tobacco," contains an alkaloid Lobeline, which is also liquid in the free condition. Its structure is unknown. The leaves and seeds of Cytisus laburnum contain the alkaloid Cytisine in considerable proportion. This is a crystalline solid, which distils under reduced pressure. It is highly soluble in water, like nicotine and lobeline, the solutions being strongly alkaline. Its constitution is imperfectly known.

With these natural alkaloids should be mentioned the synthetic quarternary ammonium bases produced by completely methylating the nitrogen of members of the adrenine series —*e. g.* p.-hydroxyphenyl ethylamine.



(Hordenine-methiodide).

The action of these is remarkably similar to that of nicotine and the others. This is the more interesting in that the complete methylation of the nitrogen atoms in nicotine itself destroys its characteristic activity.

Action.—The action of nicotine may be described for the whole group, that of the others differing only in insignificant details. The stimulant effects of nicotine on ganglion cells are observed when it is injected into the circulation in small doses. The heart is first inhibited by stimulation of the ganglion cells connected with the vagus, and then accelerated as stimulation of the accelerator mechanism gains the upper hand. The blood pressure is raised to a great height, as a result of the general stimulation of the vasomotor cells in the sympathetic ganglia. The pressor effect is evanescent. The salivary and sweat glands are excited to secretion, as are also the mucous glands of the trachea and bronchi. The pupil and plain muscle of the orbit show, in different species, a varying response, which depends on the opposing impulses from the cells in the ciliary and superior cervical ganglia, and on a third, indirect effect, which will be discussed presently. The movements of the intestine and urinary bladder show usually a brief augmentation, due to excitation of the ganglion cells connected with the vagus and the pelvic nerves, followed by inhibition, due to stimulation of sympathetic nerve-cells.

While this action on ganglion cells accounts in the main for the stimulant effects of nicotine on involuntary muscles and gland cells, there are certain effects which cannot thus be explained. In the cat, for example, the effects on the pupil and orbital plain muscle are predominantly those of the sympathetic nerve supply, and the fact that nicotine can produce such effects by action on the ganglion cells is easily proved by applying the alkaloid in dilute solution directly to the superior cervical ganglion. If, however, the ganglion be extirpated on one side, and even if the post-ganglionic fibres be allowed to degenerate completely, injection of nicotine still produces the effect of sympathetic nerve stimulation on both eyes, and the effects are practically equal on the two sides. This apparent anomaly has recently been cleared up by the discovery, that the injection of nicotine greatly accelerates the secretion of adrenalin from the suprarenal glands, and that this sudden outpouring of adrenine into the circulation is largely responsible for the production of the sympathetic effects following the injection of nicotine, and accounts for their persistence after removal of the ganglia. The same phenomenon is doubtless concerned in the cardiac acceleration which nicotine produces even after removal of the stellate ganglia.

The other alkaloids of this group also produce the effects due to stimulating all the autonomic ganglion cells, and, in addition, those due to accelerating the output of adrenalin; this gives, in the case of many organs, a preponderance of sympathetic effects over those corresponding to the cranial or sacral autonomic innervation. This preponderance is important in some cases, as in that of the bronchi; for it is to the fact that lobeline produces dilatation, a sympathetic effect, rather than constriction of these tubes, that lobelia owes its use in asthma.

In larger doses nicotine produces a secondary, paralysis of the structures which it initially stimulates. Thus, after an adequate dose of nicotine, stimulation of pre-ganglionic fibres is without effect. Stimulation of the vagus no longer inhibits the heart, stimulation of the cervical sympathetic no longer dilates the pupil. The block is in the ganglion cells, or at the synaptic junction with them of the pre-ganglionic fibres; for, if the electrodes be applied to the post-ganglionic fibres, the normal effects are still obtained. Thus if the stimulus is applied to the sinus venosus in the frog, the heart is still inhibited, and excitation of the carotid branches from the inferior cervical ganglion still dilates the pupil in the mammal. The ganglionic paralysis blocks all tonic impulses from the central nervous system to the involuntary muscles and gland cells. At this stage of nicotine action, therefore, there is a cessation of spontaneous secretions and a loss of tone of plain muscle. The blood pressure is low, and the heart-beat becomes slow and feeble, apparently on account of a direct toxic action on the heart muscle. Peripherally acting alkaloids, such as pilocarpine and adrenine, still produce their full effects, however.

Nicotine and its allies have a powerful stimulating action on the central nervous system, their injection causing muscular twitchings, hurried respiration and violent vomiting. This action soon passes over into depression, the respiration becoming slow and the reflexes depressed; the animal becomes unconscious and dies of respiratory failure. In the frog and fowl, but apparently not in the mammal, nicotine has a primary stimulant action on the skeletal muscles, by which certain muscles are preferentially affected. Larger doses produce

a curare-like paralysis of the motor end-plates, which is also seen in the mammal.

Symptoms of Poisoning.—Acute nicotine poisoning is seldom seen in man. When it occurs the symptoms include cold sweats, salivation, vomiting, purging, dyspnœa. The pulse shows stages of acceleration and of weakening and slowing. Mental confusion passes into unconsciousness, and convulsions and muscular twitchings occur, death being caused by respiratory paralysis. Cytisine poisoning is relatively common, hardly a year passing without a record of one or more cases, chiefly in children, who eat the laburnum seeds in play. Vomiting is the most constant symptom, followed by prostration and torpor; other symptoms recorded are delirium, hallucinations, mydriasis, muscular twitchings, vertigo and cold sweats. Evacuation of the stomach, warmth to the body, and caffeine to stimulate the respiration seem to be the treatment indicated.

Chronic nicotine poisoning through excessive use of tobacco, is much commoner. The usual symptoms are loss of appetite, dyspepsia, insomnia, weakness and irritability of the heart muscle, and toxic amblyopia. The effects of irritant smoke on mouth and throat can hardly be attributed to nicotine.

Therapeutic Use.—The only member of the group which is administered as a drug is lobelia, which seems to have a good effect in some cases of spasmodic asthma. Recent investigation suggests that at least part of its effect may be due to the promotion of suprarenal secretion. The drug is very variable and should be used with caution. There seems no rational basis for its preference over the other two. Cytisine, especially, which is readily obtainable pure, should be given a trial in this direction.

The wide distribution of the habit of smoking or chewing the plants containing these alkaloids is worthy of remark. No satisfactory explanation is yet forthcoming of the pleasure given by their use, nor is it clear to what extent the alkaloids contribute to the enjoyment. A certain degree of tolerance is developed to the small quantities of alkaloid absorbed; but this is very limited, and in experiments on animals no significant degree of tolerance has been obtained to doses producing definite toxic symptoms. It is stated, however, that nicotine is destroyed in the liver, and that the liver of an animal, which has been given repeated doses of the alkaloid, possesses this destructive power in enhanced degree.

Materia Medica and Preparations

Lobelia (B.P., U.S.P.).
Tinctura Lobeliæ Ætherea (B.P.).
Dose: 5–15 min. (3–10 dl.).
Tinctura Lobeliæ (U.S.P.).
Average Dose: expectorant, 15 min. (1 ml.); emetic, 1 fl. dr. (4 ml.).
Fluidextractum Lobeliæ (U.S.P.).
Average Dose: 8 min. (5 dl.).
Pulvis Lobeliæ Compositus (B.P.C.).

Curare

Curare (curara, urari, woorali) is a resinous extract prepared by certain native tribes of South America for use as an arrow poison. The composition varies, but certain species of Strychnos, Strychnos toxifera among them, are known to be used in its preparation. From different varieties of the poison Boehm prepared a series of alkaloids—curarine, protocurarine, tubocurarine, etc.—exhibiting the characteristic curare action in different degrees, and a much less toxic alkaloid, curine, with an action of different type. The action of potent specimens of curare, due to one of the curarines, is highly characteristic, its outstanding and only important feature being a paralysis of the motor end-plates of skeletal muscle; so that while impulses can travel along the nerve fibres, and the muscle fibres respond perfectly well and with practically normal contractions to direct stimulation, the impulse cannot pass from nerve fibre to muscle fibre. The result is complete paralysis of the voluntary muscular system. With small doses, such as suffice to produce this paralysis, the autonomic system is very little affected, and the fact has been much used in physiological investigation of the distribution of autonomic fibres, in nerves containing motor fibres to skeletal muscle. In large doses it paralyses also the cells of autonomic ganglia, so that the distribution of its action is similar to that of the nicotine group; it differs from these in that it acts preferentially on motor end-plates, and that its action is paralytic from the first. Curare antagonises the stimulant effect of nicotine and physostigmine on skeletal muscle.

It is stated that curare applied in large doses to the spinal medulla, so as to affect the centres before reaching the motor nerve-endings, causes an increase of reflex excitability similar to that produced by strychnine. Under ordinary conditions this is completely obscured by the peripheral paralysis.

Curare has no effect on the peripheral endings of sensory fibres; if one limb of a frog be excluded from the circulation, reflex movements in this can be excited from areas to which the poison has access. Whether it directly affects the higher centres of sensation is a matter of dispute, but the evidence is in favour of their being depressed. If artificial respiration is not applied, the paralysis of the respiratory muscles

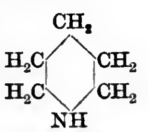
soon causes asphyxia in the warm-blooded animal.

Curarine is said to be a quarternary ammonium base, and many of the quarternary bases obtained by the methylation of alkaloids (*e.g.* methyl-strychnine) have a similar action in the frog. In this animal, however, a large proportion of ordinary alkaloids have some effect of this type when injected in large doses. In producing this effect in warm-blooded animals, in doses so small as to have no other perceptible action, the alkaloids of curare seem to stand alone. The effect is only obtained when the drug is injected hypodermically or, better, intravenously. When given by the mouth it is either absorbed so slowly that its excretion keeps pace with its entry into the circulation, or, according to some authorities, it is destroyed in the liver, so that it never reaches the site of its specific action.

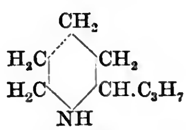
Therapeutic Use.—Curare has been tried as a means of controlling violent muscular movements and spasms—*e.g.* in tetanus; but paralysis of the respiratory muscles is separated from that of the general musculature by a dangerously narrow interval, and the drug is little used.

Coniine

Coniine is the principal alkaloid of hemlock (Conium maculatum). It is a propyl derivative of piperidine—



Piperidine.



Coniine.

which has a weaker action of the same kind, as have also methylconiine and conhydrine, which are found with coniine. Coniine is a volatile liquid with a penetrating mouse-like odour.

The action of coniine may be described as intermediate between those of nicotine and curarine; it acts more powerfully on ganglia and less on motor end-plates than curare and has more stimulant action than the latter, though less than nicotine. Thus it causes profuse salivation and sometimes sweating, and a considerable rise of blood pressure; but these effects more rapidly give way to ganglionic paralysis than effects of equal intensity produced by nicotine. In the frog a curare-like paralysis of motor end-plates is the predominant feature in the action, but in the mammal these structures seem to be more resistant to coniine, as to so many alkaloids. It is uncertain how far the final respiratory paralysis, which it causes in mammals, is due to peripheral, how far to central paralysis. The autonomic ganglia are paralysed, so that stimulation of the vagus and cervical sympathetic are no longer effective on the heart or the pupil. Large doses apparently depress the heart muscle, like large doses of nicotine.

Symptoms of Intoxication.—Poisonous doses cause drowsiness, staggering gait, and muscular weakness; the ocular muscles are especially susceptible. Nausea and vomiting, with profuse salivation, occur. The pupils are moderately dilated. Muscular tremors and convulsions are recorded, and seem to indicate central excitation; but this soon gives way to the dominant phase of depression, death being due to respiratory failure, in which, as stated, peripheral paralysis of motor end-plates probably plays a large part. The mind remains clear to a late stage of the poisoning, as in the historic case of Socrates.

Therapeutics.—It is doubtful whether conium or coniine has any therapeutic value, and they are hardly ever used. The British Pharmacopœia of 1914 no longer includes them.

Materia Medica and Preparations

Conii Fructus (B.P., 1898.). Conium (U.S.P.).
- Tinctura Conii (B.P., 1898.). ½–1 fl. dr. (2–4 ml.).
- Fluidextractum Conii (U.S.P.).
  Average Dose: 3 min. (2 dl.).

Conii Folia (B.P., 1898.)
- Succus Conii (B.P., 1898.). 1–2 fl. dr. (4–8 ml.).
- Unguentum Conii (B.P., 1898.).

Gelsemium and Gelseminine

Gelseminine is an amorphous alkaloid contained in the root of the yellow jasmine, Gelsemium nitidum or sempervirens. In the same drug occurs Gelsemine, an alkaloid forming crystalline salts; this has a strychnine-like action on the frog, but produces no effect of any importance in the mammal, so that it has no practical significance.

Gelseminine has a general action almost identical with that of coniine, but it is said that the paralytic effect on the centres plays a larger, that on the motor terminations a smaller part in the effect than in that of coniine. It has, in addition, a power of paralysing the sphincter of the pupil and the ciliary muscle, when applied to the conjunctiva. The action is apparently similar to that of atropine, but much weaker; non-fatal doses of gelseminine are not able to produce the effect through the general circulation.

Therapeutic Use.—Gelsemium is said to be of value in trigeminal neuralgia, and the tincture is not infrequently prescribed in this condition. The nature of the action is obscure.

As a mydriatic gelseminine has no value in comparison with the atropine series, being much more irritant to the conjunctiva.

Materia Medica and Preparations

Gelsemii Radix (B.P.). Gelsemium (U.S.P.).
Tinctura Gelsemii (B.P., U.S.P.). 5–15 min. (3–10 dl.).
Fluidextractum Gelsemii (U.S.P.).
Average Dose: 1 min. (5 cl.).

Scoparius and Sparteine

Sparteine is an alkaloid found in broom-tops, the slender branches of Cytisus Scoparius. It is, like coniine, a liquid, volatile alkaloid, forming crystalline salts. Its action is very similar to that of coniine and gelseminine, but much weaker, and it has very little effect on the centres, its action in large doses being, predominantly, a paralysis of autonomic ganglion cells and motor end-plates. When given intravenously it causes a small rise of blood pressure, soon neutralised by slowing and weakening of the heart-beat. Its supposed resemblance to digitalis in action is purely illusory, and it has no directly beneficial effect on the heart.

Therapeutic Use.—Sparteine has probably no therapeutic value. The infusion of broom is diuretic, and owes this action to a phenolic substance *scoparin.* The drug should properly be classed with diuretics, such as Uva Ursi.

Materia Medica and Preparations

Scoparii Cacumina (B.P.). Scoparius (U.S.P.).
Infusum Scoparii (B.P.). 1–2 fl. oz. (30–60 ml.).
Succus Scoparii (B.P.). 1–2 fl. dr. (4–8 ml.).
Sparteinæ Sulphas (U.S.P.).
Average Dose: $\frac{1}{5}$ gr. (10 mg).

H. H. D.

DRUGS PRODUCING CONVULSIONS

Strychnine.—The first place as the head of the family of convulsants has been assigned, and rightly so, to Strychnine. The British Pharmacopœia, while specifying nux vomica as the chief source, permits the extraction from other species of Strychnos, which therefore includes—

Strychnos Philippenses Blanco
Strychnos Colubrina
Strychnos Tieuté Lesch
Strychnos Ignatii Bergius

The last, according to Murray, arrived in Europe from the Philippines, through the agency of the Jesuits who, on account of its virtues, bestowed on it the name of the head of the order, St. Ignatius. Bohn of Leipzig introduced the bean into Germany about the same period. Nux vomica seeds were introduced into English shops about 1640. These are disc shaped, nearly one inch in diameter and one quarter of an inch in thickness.

Strychnine is not confined to the seeds, but is met with in the wood and bark. The St. Ignatius bean yields strychnine more easily and largely than nux vomica. The B.P. omits the process of extraction of the alkaloid for the simple reason that it can only be carried out profitably by the manufacturing chemist on a large scale. The alkaloid is associated with another termed Brucine, and these are present in the proportion of 1·84 to 5·3 per cent., 2·8 being an average percentage. Sometimes the two are present in nearly equal proportions. Since brucine is less poisonous than the other, the amount of total alkaloids affords a somewhat uncertain standard from a medicinal point of view, so in the standardisation of nux vomica the proportion of strychnine is usually determined as distinct from total alkaloid.

Strychnine is officially described as colourless, inodorous, transparent, prismatic crystals, or a white crystalline powder with a bitter taste which is perceptible in a solution of 1–700,000. It is permanent in the air, and should, like dilute hydrocyanic acid, be tasted with caution. It is soluble in six parts of chloroform, one hundred and fifty of benzine, and six thousand four hundred of water. Sulphuric acid forms a colourless solution with it, indicating absence of sugar and other readily carbonisable organic impurities, while nitric acid when added to it on a white porcelain surface should produce no colour, or no more than a faintly pink coloration, indicating the absence or mere trace of brucine. The likely impurities are, besides brucine, colouring matter, lime or magnesia. These two latter remain behind when the drug is incinerated in the open air, whereas pure strychnine leaves no residue under such conditions. The absence of colour reaction with nitric and sulphuric acids distinguishes strychnine from several other alkaloids.

The usual antidote is permanganate of potash, with a dilute solution of which the stomach should be washed out, after giving chloroform as an anæsthetic. Spinal sedative treatment is continued by means of chloral hydrate, opium, bromides in half-ounce doses, also amyl nitrite. A. E. Russell advises injection of cocaine into the spinal theca. The differential diagnosis of poisoning rests on the jaw being affected after the limbs and trunk, the relaxation between the convulsions, the rapid onset of the attack and the retention of consciouness.

Pharmacology.—Strychnine is a powerful antiseptic agent, but is a dangerous one and is readily absorbed from wounded surfaces. Internally it possesses all the properties of the class of Bitters, and even extremely dilute

solutions show this property markedly. It is, however, a flavourless bitter, and this fact, together with the persistence of its taste, makes it more useful as an adjuvant in a bitter mixture rather than as the main bitter drug. It increases intestinal peristalsis quite distinctly. It is easily absorbed from mucous surfaces and reaches the blood in this manner or by hypodermic injection, and causes an increase in metabolic processes and elevates body temperature. Reaching the tissues it tends to be held somewhat closely by them and is not quickly excreted. Accordingly a cumulative action is often set up even by small doses, when such are given over a lengthy period. More particularly does it linger in the nervous tissues, and some persons appear to be more sensitive to strychnine than others, possibly on account of the closer and more lasting alliance between their tissues and the drug. Small doses stimulate the special senses, causing greater keenness of smell and taste, while colour and light perception may be increased; even the field of vision may be extended. In larger doses it will cause stiffness and rigidity of muscles and a notable heightening of reflex excitability. The anterior cornu motor cells are stimulated and the intraspinal reflex paths are more ready to receive and transmit impressions. Any stimulation from the outside, be it transmitted along special or common sensory nerves, results in motor excitation, which may be so pronounced as to result in convulsion. Strychnine stimulates the medullary grey matter, the respiratory, cardiac, and vasomotor centres being involved. For long the action of the drug upon the heart, through the cardiac centre, has been regarded as powerful and important, but the opinion of Cushny, expressed many years ago, that the drug did not act strongly upon the mammalian heart, has received lately some confirmation in the investigation by Parkinson and Rowlands (*Quart. Journ. of Med.*, October 3, 1913). These observers find that in cardiac failure, and auricular fibrillation, strychnine has no beneficial action as a rapid cardiac restorative, although they express no opinion as to the action of the drug as a cardiac tonic. It is possible that the raising of blood pressure under strychnine may be due to the rise of pressure coinciding with the excessive muscular contractions induced by the drug, and in support of this is the fact, long known, that when the muscles are curarised strychnine may cause slowing of the heart.

Fraser and Crum Brown have shown that the ethyl and methyl combination of strychnine have an opposite effect to strychnine, and while the latter stimulates reflex action these compounds reduce or abolish it.

Therapeutics.—Strychnine as existing in nux vomica is the most extensively used drug. It is one of the most powerful and constant stimulants to the respiratory centre. In pneumonia it is administered as such, as a tonic to the general nervous system, as a heart stimulant to prevent or assuage the troublesome abdominal distension. Combined with digitalis for acute heart failure it causes slowing of the heart and so increases the period of physiological rest. Strychnine may also help in the failure which occurs in bradycardia.

The consensus of opinion places strychnine after digitalis in heart disease; an exception occurs in fatty myocarditis. According to Hale White strychnine seems to have its action by rise of blood pressure, while digitalis acts on the heart muscle.

In sea-sickness it has lately been invoked, also in the more serious condition of whooping-cough. In congenital heart disease it comes first in order of treatment. For the severe vomiting associated with infantile diarrhœa, it is given in doses of $\frac{1}{300}$ gr. hypodermically, with or without injection of camphorated oil.

For diphtheric paralysis adrenalin chloride has to some extent supplanted its use, as strychnine is by no means free from danger in this condition.

It lowers the resistance to the passage of a nervous impulse, and in larger doses replaces reflex inhibition by contraction.

Strychnine acts on the gastric mucous membrane, and also excites the vasomotor and motor centres of the spinal cord, and so increases the activity of the circulation and general systemic tone, hence it acts as a valuable tonic. Given along with iron and a bitter in anæmia, it is useful especially in cases of general loss of tone. It is used in paralysis, but as in such the loss of muscular power is less seldom due chiefly to depression of spinal centres, it is not common to obtain much benefit from it. Some authorities recommend it in infantile paralysis, and when muscular nutrition is at fault advise its injection into affected parts. When administered in post-hemiplegic conditions in full doses, twitching will appear first in the paralysed muscles as opposed to those under the control of the will. In poisonous doses the convulsions produced are usually tonic or continuous, in contradistinction to poisons like tetanus where the spasms are clonic, that is to say, with a period of rest or relaxation between. At the same time it should be noted that the convulsions with strychnine poisoning may be both tonic and clonic. During the convulsions, consciousness is undisturbed. The body is rigid, and the face drawn, giving rise to the expression "risus sardonicus." The limbs are partially or wholly extended and the back bent in opisthotonic posture. The convulsions

are painful, and death may occur in them due to asphyxia or exhaustion.

Preparations

As regards those of Nux Vomica the seeds themselves are now standardised to contain not less than 1·25 per cent. of strychnine. The Extractum Nucis Vomicæ Siccum, *Dose* $\frac{1}{4}$–1 gr. (16–60 mg.), is slightly modified, but is of the same strength as previously, the modification consisting in the use of calcium phosphate instead of milk sugar as a diluent. The Extractum Liquidum, *Dose* 1–3 min. (6–18 cl.), remains the same, whilst the Tinctura, *Dose* 5–15 min. (3–10 dl.), is about half the strength of the B.P. 1898 Tincture. It is now required to contain not less than 0·12 per cent., nor more than 0·13 per cent., by volume of strychnine, whereas the B.P. 1898 Tincture was required to yield not less than 0·24 nor more than 0·26 g. of strychnine in each 100 c.cm.

Strychnine is usually prescribed in the form of the Liquor, which contains one grain of the hydrochloride in 110 minims. It is prudent not to combine it in mixture form, but to give it alone. If ordered with bromides, or iodides, a corresponding salt of hydrobromide, hydroiodide, is produced. A common error is to prescribe it with iodide of potassium, when precipitation follows, and the patient may receive the whole of the strychnine in one dose at the last. Similarly, if given with Liquor Arsenicalis the alkaloid is precipitated, for no alkali can be associated with the Liquor. The Liquor Arsenici Hydrochlor. must be used instead. Bicarbonate of soda is generally thought to be incompatible, but the soda, if present in a certain quantity, does not precipitate the alkaloid. It is better, however, to avoid alkalies. If prescribed with Spt. Ammon. Aromat. and Spt. Chloroformi, part of the chloroform may be deposited, carrying down with it some of the strychnine which had been liberated by the ammonia. If the bottle is shaken before each dose there is less risk, but it is wiser to give the strychnine alone. Liq. Strychninæ, it is interesting to note, first became official in 1898.

Owing to the presence of alcohol the liquor is not used for hypodermic medication.

Strychnine may be conveniently ordered in combination with iron and quinine in the scale preparation, which may be dissolved and given as a mixture, or massed into pills with alcohol. The dose of the salt is 2–5 gr.

Strychnina (B.P., U.S.P.).
Dose : $\frac{1}{64}$–$\frac{1}{16}$ gr. (1–4 mg.).

1. Syrupus Ferri Phosphatis cum Quinina et Strychnina (B.P.). Syrupus Trium Phosphatum, Easton's Syrup (about 1 in 2000).
Dose : $\frac{1}{2}$–1 fl. dr. (2–4 ml.).
2. Elixir Ferri Quininæ et Strychninæ Phosphatum (U.S.P.).
Average Dose : 1 fl. dr. (4 ml.).
3. Syrupus Ferri Quininæ et Strychninæ Phosphatum (U.S.P.).
Average Dose : 1 fl. dr. (4 ml.).
4. Glyceritum Ferri Quininæ et Strychninæ Phosphatum (U.S.P.).
Average Dose : 1 fl. dr. (4 ml.).
5. Pilulæ vel Tablettæ Ferri Phosphatis cum Quinina et Strychnina (B.P.C.). These pills or tablets may be ordered instead of Easton's Syrup; each corresponds in strength to 1 fl. dr. of the Syrup.
Dose : 1 tablet.
6. Syrupus Triplex (B.P.C.) consists of equal parts of Syrupus Ferri Phosph. Co., Easton's Syrup, and Syrupus Hypophosphitis Co.
Dose : $\frac{1}{2}$–1 fl. dr. (2–4 ml.).
7. Syrupus Ferri Bromidi cum Quinina et Strychnina (B.P.C.).
Dose : $\frac{1}{2}$–1 fl. dr. (2–4 ml.).
8. Pilulæ Aloini et Strychninæ Compositæ (B.P.C.). $\frac{1}{50}$ gr. in each.
Dose : 1–2 pills.

Strychninæ Hydrochloridum (B.P.).
Dose : $\frac{1}{64}$–$\frac{1}{16}$ gr. (1–4 mg.).

1. Liquor Strychninæ Hydrochloridi (B.P.). 1 per cent.
Dose : 2–8 min. (12–50 cl.).
2. Injectio Strychninæ Hypodermica (B.P.). 0·75 per cent. in distilled water recently boiled and cooled.
Dose : hypodermically 5–10 min. (3–6 dl.).
3. Mistura Strychninæ Acida (B.P.C.).
Dose : $\frac{1}{2}$–1 fl. oz. (15–30 ml.).
4. Elixir Formatum Compositum (B.P.C.). Contains 2·08 per cent. Liq. Strych. Hydrochlor.
Dose : 1–2 fl. dr. (4–8 ml.).
5. Elixir Pepsini et Bismuthi cum Strychnina (B.P.C.).
Dose : $\frac{1}{2}$–1 fl. dr. (2–4 ml.).
6. Elixir Pepsini et Bismuthi et Strychninæ cum Ferro (B.P.C.).
Dose : $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

Strychninæ Nitras (U.S.P.).
Average Dose : $\frac{1}{64}$ gr. (1 mg.).

Strychninæ Sulphas (U.S.P.).
Average Dose : $\frac{1}{64}$ gr. (1 mg.).

1. Injectio Strychninæ Hypodermica (B.P.C.). 0·4 per cent.
Dose : 2–8 min. (12–50 cl.).

Ferri et Strychninæ Citras (U.S.P.).
Dose : 1–3 gr. ($\frac{1}{2}$–2 dg.).

Ferri Quininæ et Strychninæ Citras (B.P.C.).
Dose : 2–5 gr. (1–3 dg.).
Strychninæ Formas (B.P.C.).
Dose : $\frac{1}{64}-\frac{1}{16}$ gr. (1–4 mg.).

Brucine, already stated as occurring in varieties of Strychnos, along with Strychnine, was first discovered in the bark called false Angostura, in combination with gallic acid, while in strychnos it is combined as an igasurate. It is without odour, but has a harsh, bitter taste. It dissolves in 850 parts of cold, and 500 of boiling water, very soluble in alcohol. It forms crystallisable salts with acids. Concentrated nitric acid gives with brucine and its salts an intense crimson colour, changing to yellow with heat, and with stannous chloride yields a purple reaction. Sulphuric acid, followed by bichromate of potassium, develops a red or reddish brown colour, passing to green and yellow. Cotton's test is to add to a warm solution of Brucine in nitric acid, a concentrated solution of hyposulphite of soda. The result is first violet, then green.

In the beauty and quickness of its reactions with liquid tests, brucine is second only to strychnine. Brucine is much less rapidly absorbed than strychnine, and is forty to fifty times less powerful as a convulsant, but more poisonous to the sensory nerves than the latter alkaloid. Mays found that a 5 to 10 per cent. solution of chemically pure brucine applied to the mouth of a man caused rapid loss of sensibility, and he asserts that a 20 per cent. solution is capable of exerting a decided local anæsthetic action when placed on the skin. For itching of chronic pruritus Zeiss and Burnett give a 5 per cent. solution as a local application in inflammation about the external ear. Some authorities hold that it acts more favourably as a bitter in the stomach, probably because it is more slowly absorbed, and acts locally more persistently. The dose of brucine is $\frac{1}{12}-\frac{1}{2}$ gr.

Picrotoxin (B.P., 1898) is the best-known member of a group of convulsive poisons resembling each other closely in action, but of whose chemistry little is known beyond the fact that they are devoid of nitrogen. It is a crystallisable substance occurring in the seeds of Cocculus Indicus or Anamirta paniculata to an extent of $\frac{2}{3}$ to 1 per cent., and is the source of the poisonous property of the drug. It does not neutralise acids, it is soluble in water and in alkalies. In its reaction to chemical tests it somewhat resembles strychnine. In man the drug acts as it does on the lower animals. In large doses it causes intense excitement of the motor cells in the spinal cord medulla, it acts on the vasomotor and respiratory centres, while in some cases serious and even fatal poisoning has been produced by it. The convulsive attacks are both epileptic and tetanic, and a feature of the movements is their purposiveness, partaking, it may be, of the nature of walking, eating, etc., sometimes vomiting.

In Europe it has been stated to be added to malt liquors to give them bitterness and intoxicating properties. While strychnine acts chiefly on the cord, picrotoxin has a selective action on the medulla.

Given internally it slows the heart, due to stimulation of the inhibitory centre in the medulla, the arterial tension is raised by stimulation of the vasomotor centres in the medulla. Respiration is accelerated before the convulsions appear, later on it may become slow and laboured, due perhaps to central paralysis; the vomiting referred to above is probably of central origin, and not due to gastric irritation. Crichton Browne has shown that in rabbits the effects are completely counteracted by subcutaneous injection of chloral hydrate. Its use has been suggested in epilepsy, hystero-epilepsy and chorea, but it is used principally to check the profuse night sweats of phthisis, through its action in accelerating respiration, thus removing the partial asphyxia and so preventing stimulation of the nervous mechanism governing perspiration. It is best administered in pills, the drug being triturated with milk, sugar, and massed with glycerine of tragacanth. A solution in water (1–400) is used as a hypodermic injection. The dose of picrotoxin is $\frac{1}{100}-\frac{1}{30}$ gr.

Camphor (B.P., U.S.P.) belongs to the class of bodies known as stearoptenes, that is, the solid portion of a volatile oil. It comes mostly from the Island of Formosa and Japan. The wood is cut into strips, then exposed to the vapour of boiling water, when the camphor, which volatises with the steam, is collected. Afterwards it is placed in vats for export, when a yellow, essential oil drains out. This oil is much used by the Chinese for rheumatism.

By treatment with various reagents, a number of interesting products are obtained, such as monobromated camphor got by heating camphor and bromine in a sealed tube. This body was formerly much used in nervous depression and pain of epidemic influenza, for lumbago, whooping cough, chorea, epilepsy and petit mal. Such is best given in 5 gr. pills.

The exact action on the cord in man is not yet finally determined. The convulsions are not due to any action on the cord, but to stimulation of the higher areas. The cerebral cortex is involved in the action. The loss of consciousness, the stupor and coma observed, would indicate a final paralysis of the cerebral cortex.

Taken as a poison the symptoms begin with languor, giddiness, dimness of vision and

confusion of intellect, followed by depression, intoxication or violent delirium.

Camphor in 2-grain doses has been given for erysipelas, also in the hæmatemesis following gastric ulcer, while combined with digitalis to increase diuresis, it has been tried to aid elimination in post-partum eclampsia. Carschmann's solution, camphor 2 parts, ether 3 parts, olive oil 10 parts, is often used as a cardiac stimulant in acute fevers, such as pneumonia, in doses of ♏ 10 four-hourly.

The official preparations are—

I. *Camphor Water* (B.P., U.S.P.).—Is used chiefly as a flavouring agent, but it possesses a mild carminative and expectorant action. It has been used as a preservative in the hypodermic injections of ergotin and apomorphine.

II. *Liniment of Camphor* (B.P., U.S.P.).—Is a useful counter-irritant for the chest in the bronchitis of children; if some turpentine or eucalyptus oil be added it increases its action. It serves as an antidote for carbolic-acid poisoning. A 10 per cent. solution injected subcutaneously has been suggested by Volland in phthisis where there is cardiac weakness. Camphorated oil (1–15 or 1–30) in ♏ 5 doses, associated with gr. 1 in 100 strychnine, injected subcutaneously has much value in the collapse following acute diarrhœa in children.

III. *Compound Camphor Liniment* (B.P.).—The strong ammonia is used in this preparation, hence its action is that of powerful counter-irritation. It is used for chest complaints, chronic rheumatism, etc. In the new B.P. there is less oil of lavender.

IV. *Spirit of Camphor* (B.P., U.S.P.).—Is given in sugar as a diaphoretic, for catarrh of the nose, etc. A stronger solution used for similar purposes is the well-known Rubini's essence.

The ordinary spirit of camphor in ♏ 5–10 is given to children for the collapse consequent in acute diarrhœa. Sprinkled on cotton wool it forms a favourite application to the chest in pneumonia of children.

V. *Compound Camphor Tincture* (B.P.).—Contains opium in the strength of gr. $2\frac{1}{5}$ to the ounce. Each ʒi contains $\frac{1}{37}$ grain of morphine. An imitation of the tincture with the opium excluded constitutes Compound Camphor Spirit.

Camphor is a constituent in nine official liniments and one ointment, viz. Scott's Dressing.

It is also contained in the following additional preparations—

(*a*) A concentrated water.

(*b*) Camphorated chloroform. When camphor is dissolved in chloroform, the preparation is largely used in toothache.

(*c*) Camphor ointment. A mild counter-irritant and analgesic.

(*d*) Camphor ointment, hard. The well-known camphor ice.

Camphor rubbed in a warm mortar with certain drugs produces liquids which are soothing external applications, such are camphor and chloral, camphor and phenol, etc.

D. M. M.

HYPNOTIC AND NARCOTIC DRUGS

A convenient practical distinction may be drawn between the hypnotic and narcotic drugs. The former are distinguished by their power of producing sleep (ὑπνόω = to put to sleep), and have little or no action in allaying pain. They are all synthetic chemical products and vary considerably in structure. The latter are primarily characterised by their power of abolishing pain (ναρκόω = to benumb or deaden), though secondarily they produce sleep; they are mainly bodies of an alkaloidal character, and those whose structure is approximately known closely resemble each other. In their physiological action these two groups show certain well-marked differences. Speaking generally the hypnotic drugs depress the sensory cells and have no special action on the algesic areas of the brain; in larger doses they depress the motor cells, both of the brain and cord. The narcotic drugs also depress the sensory cells, but have a specially marked action on the algesic areas, and in larger doses produce motor excitation similar to that produced by strychnine. The hypnotic drugs are mainly excreted in the urine, the narcotics by the bowel. The excitement produced by hypnotic drugs is generally attributed to loss of higher control or paralysis of the psychical centres. The convulsions produced by the narcotics, on the other hand, are due to some actions on the cord, the exact mechanism of which is at present only capable of hypothetical explanation.

Further comparison of the two groups is hardly possible, as there are considerable variations in the action of the synthetic hypnotics, depending on the chemical group to which they belong. These will, therefore, be described in detail later, when these groups are separately considered.

The Synthetic Hypnotics.—The general indications for the use of one of this series of drugs are the insomnia occurring in acute diseases, the insomnia depending on psychical causes, such as worry, over-work or strain, mental diseases associated with excitement, and delirium tremens. The employment, however, of a hypnotic in any individual case must be a matter for careful consideration, in view of the ease with which a drug habit may be set up, especially in those cases where a recurring cause may frequently produce inability to sleep. Probably, therefore, the largest experience in the clinical use of hypnotics is to be gained in asylums for

the insane, where the necessity is often urgent, and the contra-indications of less import.

The ideal hypnotic should be a pure chemical substance, and not easily decomposed or altered by light, warmth or other ordinary external conditions. It should be easily soluble, not unpleasant to taste, rapidly absorbed, and completely eliminated, so that its action in the body may be immediate and not cumulative. It should act solely on the higher cerebral cells, and produce no undesirable effects on the heart, digestive organs or general metabolism. The sleep produced should be natural, refreshing and dreamless.

No known drugs fulfil all these conditions completely, and although the multiplication of synthetic remedies has not, as a rule, added much which is of value to our resources in treatment, it must be allowed that with regard to the hypnotics there are certain advantages in the large choice of drugs which modern chemistry has placed at the disposal of the physician. In the first place, the varying potency of these substances allows of easy graduation, according to the severity of the case, without resort to very large or very small doses. In the second place, in cases where a hypnotic has to be employed for a lengthened period, the tolerance which is almost invariably acquired to any given drug may be avoided by alternating it with another of a different class; and, in the third place, as all hypnotics have certain physiological contra-indications, but not necessarily the same, it is possible to choose one which is most suited to a particular individual, with regard to the special by-effects which it is desired to avoid.

It must, however, be emphatically stated here that there is no hypnotic drug which is incapable of producing a habit or craving in some patients, which will, if once acquired, lead to self-medication in increasing doses, and eventually, in all probability, to moral and physical disaster. Manufacturers are too fond of announcing that their new hypnotic has never been observed to create a habit, but these statements are usually made early in the career of a synthetic drug, before it has become widely used or popularly familiar. Even the extraordinarily nauseous paraldehyde has been known to set up a "paraldehyde habit." Two cases, not fatal, developed symptoms resembling those of chronic alcoholism; in a third case about 3½ oz. taken in the course of thirty-three hours proved fatal.

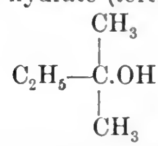
Administration of Hypnotics. — No hypnotic should ever be given in a solid form, such as a tablet, as in this case great delay may occur in the absorption of the active principle. Those which are insoluble in cold water should be given in hot fluids or dilute alcohol, and, if not completely dissolved, at least in suspension. Where capsules or cachets are used, they should be followed by a draught of warm fluid. Time for the drug to act must be allowed, according to the rapidity of absorption. The average time in which sleep may be expected will be noted in the description of the individual drugs later. When a drug is not readily excreted, a smaller dose should be given if it has to be repeated on the subsequent night, as probably some of the original quantity is still in the tissues. The same rule applies where a second dose is required on the same night.

Chemical Classification of Hypnotics.—Hypnotics having similar chemical structure act in a similar way; they may be arranged as follows—

(1) *Alcohols*—

Ethyl alcohol, $CH_3.CH_2.OH$.

Amylene hydrate (tertiary amyl alcohol),



Hypnotic action mild. Gastric irritants.

(2) *Aldehydes*—

Paraldehyde $(CH_3.CHO)_3$

A polymer of ordinary aldehyde, similar in action to alcohols.

(3) *Ketones*—

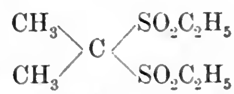
Propion (diethyl ketone), $C_2H_5.CO.C_2H_5$.

Hypnone (benzoyl methyl ketone), $C_6H_5.CO.CH_3$.

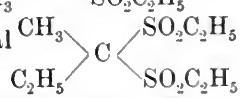
Similar in action to alcohols.

(4) *Sulphones*—

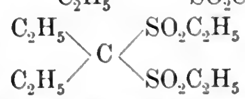
Sulphonal,



Methylsulphonal or Trional,



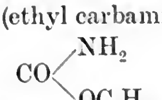
Tetronal,



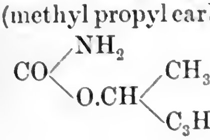
Hypnotic action and toxicity increases with number of ethyl groups, and is also conditioned by their place in the molecule. Slowly absorbed and excreted; gastro-intestinal irritants; produce hæmatoporphyrinuria

(5) *Urea derivatives*—

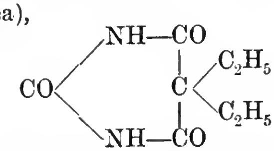
Urethane (ethyl carbamic ester),



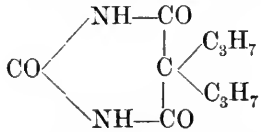
Hedonal (methyl propyl carbinol urethane)



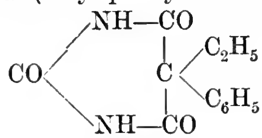
Barbitonum, Veronal (diethyl malonyl urea),



Proponal (di-propyl-malonyl-urea),



Luminal (ethyl phenyl malonyl urea),



Diuretic bodies, slowly absorbed (except urethane), and not very rapidly excreted. Excretion much hindered by renal disease.

(6) *Halogen-containing substances*—

Chloral hydrate, $\mathrm{CCl_3CH}\Big\langle\begin{matrix}\mathrm{OH}\\ \mathrm{OH.}\end{matrix}$

Chloralose, $C_6H_{10}O_5.CCl_3.CHO$.

Chloralamide (chloral formamide),

$$\mathrm{CCl_3CH}\Big\langle\begin{matrix}\mathrm{OH}\\ \mathrm{NH.OCH.}\end{matrix}$$

Isopral (trichlor-isopropyl-alcohol), $C.Cl_3.CHOH.CH_3$.

Chloral urethane,

$$\mathrm{C.Cl_3CH}\Big\langle\begin{matrix}\mathrm{OH}\\ \mathrm{NH.CO.OC_2H_5.}\end{matrix}$$

Bromal, CBr_3CHO.

Bromural (mono-brom-isovaleryl-urea),

$$\begin{matrix}\mathrm{CH_3}\\ \mathrm{CH_3}\end{matrix}\Big\rangle\mathrm{CH.CHBr.CONH.CONH_2.}$$

Neuronal (diethyl-brom-acetamide),

$$\begin{matrix}\mathrm{C_2H_5}\\ \mathrm{C_2H_5}\end{matrix}\Big\rangle\mathrm{CBr.CONH_2.}$$

Adalin (mono-brom-diethyl-acetyl-urea),

$$\begin{matrix}\mathrm{C_2H_5}\\ \mathrm{C_2H_5}\end{matrix}\Big\rangle\mathrm{CBrCO.NH.CO.NH_2.}$$

The hypnotic action in part depends on the halogen, which also acts as a cardiac depressant.

Therapeutic Classification of Hypnotics.—Knowledge of the chemical structure of an hypnotic does not enable us to compare it practically with one of another group. For therapeutical purposes a different classification will be found of more practical value. The following grouping is based on the author's personal experience. The published literature has also been reviewed, especially as regards fatalities and toxic effects.

Group I.—Hypnotics of Doubtful Value

Tetronal, though more powerful, is also more dangerous than the other sulphones. Dose 10–20 gr. (0·6–1·2 gm.).

Isopral has a markedly depressant action on the heart, an unpleasant taste, lowers the blood pressure and irritates the stomach. It is not a very powerful hypnotic, and tolerance is soon established. Dose 8–15 gr. (0·5–1 gm.).

Chloralose resembles chloral in action, but is more irritant to the stomach. It is unstable, polymerising to parachloralose, which is not hypnotic, and may be the cause of the toxic symptoms. It produces intoxication, increased reflexes and convulsions. Dose 2–8 gr. (0·13–0·5 gm.).

Chloralurethane (*ural, uralium*) is also sold in alcoholic solution as *somnal.* It is an uncertain hypnotic, a gastro-intestinal irritant and liable to produce toxic symptoms. Dose 15–45 gr. (1–3 gm.).

Propion is insoluble, disagreeable and not powerfully hypnotic. *Hypnone* is unreliable and liable to produce headache. Neither have been at all widely used.

Butyl chloral acts similarly to chloral, and is even nastier. *Trigemin*, a compound of this drug with pyramidon, is no improvement on the latter. Neither drug acts specifically on the fifth nerve.

Hypnal is merely a compound of chloral and antipyrin. *Viferral*, another chloral compound, is nasty and has no advantages of importance over other mild hypnotics.

Dormiol, a compound of chloral and amylene hydrate, is also nasty and somewhat toxic. It irritates the stomach, and its hypnotic action diminishes rather rapidly.

Group II.—Powerful Hypnotics

Chloral Hydrate, often called chloral for short, is a crystalline substance, soluble in water, possessing an unpleasant taste and odour. The dose is 5–20 gr. (0·3–1·2 gm.). It is easily absorbed, and circulates in the blood unchanged. It is eliminated partly unchanged and partly reduced and combined with glycuronic acid as urochloralic acid. It depresses the higher cerebral centres, producing sleep, in moderate doses, which lasts for six to eight hours. It is an irritant, and may set up nausea and vomiting. It depresses the respiratory, cardiac and vasomotor centres, and in cases of poisoning the respiration usually fails first; it also has a direct action on the cardiac muscle similar to that of

other chlorine compounds, such as chloroform. Metabolic processes are diminished. When given in large doses or intravenously it produces complete surgical anæsthesia, but such a proceeding is distinctly dangerous.

Chloral hydrate has now been used in practice for nearly half a century, and is probably still the most generally useful of the more powerful hypnotics. It has little effect in cases where severe pain is present, but is, on the whole, reliable. Its disadvantages are its unpleasant taste, its liability to cause nausea, and, more particularly, its depressant action on the heart. For this reason it is contra-indicated by the presence of cardiac weakness. It is well borne by children, to whom it is best given by the rectum. At one month 1 gr. may be given in this way, and at one year 3–5 gr., and the dose repeated in a few hours as required.

Methylsulphonal, or *Trional*, is a crystalline powder not very soluble in water. The dose is 10–20 gr. (0·6–1·2 gm.). It acts in half an hour to an hour, and is more rapidly eliminated than sulphonal, causing no persistent drowsiness on the following day. It is fairly reliable, except in the presence of pain or extreme excitement. Its disadvantages are its varying toxicity to different individuals and its action as a blood poison (*v. s.*). Three grams (45 gr.) have proved fatal in one case, whereas in another 180 gr. (12 gm.) were taken with no further result than prolonged sleep. Women are less tolerant than men, and anæmic, cachectic persons than those who are well nourished.

Neuronal, a crystalline powder, is slightly soluble in water, readily in alcohol. It has a faint odour and bitter taste and is decomposed by alkalies. The dose is 8–15 gr. (0·5–1 gm.), but in severe cases larger amounts are necessary (45 gr. or 3 gm.). It is a powerfully hypnotic drug, acting in twenty to thirty minutes, but the sleep produced is deep and heavy, and after-effects are not uncommon. It is, moreover, a cardiac depressant and an irritant to the gastro-intestinal tract. Tolerance is somewhat rapidly established.

Barbitonum, or *Veronal*, is a crystalline, slightly bitter, powder, not very soluble in cold water, more so in hot water or alkalies. It must not be given in milk, as an unpleasant bitter taste is produced. The dose is 5–10 gr. (0·3–0·6 gm.), but larger doses, up to a maximum of 15 gr. (1 gm.) have been given. Veronal is a powerful hypnotic, and in somewhat large doses will produce sleep in alcoholic delirium or in presence of pain where other drugs fail. It is, however, unsuitable for general use owing to the toxic symptoms which may occur even with small doses. The smallest fatal dose recorded is 15 gr. (1 gm.), but the writer knows of an unpublished case in which 8 gr. were fatal. Two cases have been recorded in elderly women in which 5 gr. caused prolonged drowsiness and apparently transient hemiplegia. Small doses have also been observed to cause circumscribed patches of dermatitis, which persisted as long as the drug was continued, and recurred each time it was taken. Large doses, though producing severe and alarming symptoms, have been recovered from, but I have found no case recorded of recovery after more than 150 gr. (10 gm.).

The toxic symptoms are abdominal pain, sweating, pyrexia, suppression of urine or diuresis, and somnolence deepening to coma. In slighter cases there may be nausea, vomiting, headache, dizziness, drowsiness, ataxia and various skin rashes. Hæmaturia may occur and hæmatoporphyrinuria is said to have been noticed. Experimentally the drug produces vasomotor paralysis of peripheral origin in animals. In chronic poisoning, ataxia, convulsions, cyanosis and collapse, or a symptom-complex suggesting alcoholic poisoning, have been described. The treatment must be on general lines to secure elimination and stimulate the system. It must always be remembered that owing to the insoluble nature of veronal, it may remain in the stomach for some time, so that it is always worth while to wash out the stomach.

Medinal is a sodium compound of veronal, and is soluble. As the reason why veronal does not oftener cause toxic symptoms is, partly at any rate, the fact that it is insoluble and slowly absorbed, medinal must be regarded as a still more dangerous drug. *Proponal* is very similar to veronal in every respect, but is more powerful and far more toxic. *Luminal* appears to be very similar to proponal, but it has not been used for a sufficiently long time for a final opinion on its value. The dose is small, 3–5 gr. (0·2–0·3 gm.).

Group III.—Medium Hypnotics

Sulphonal, a stable, crystalline, somewhat insoluble substance, possessing neither taste nor odour. Dose: 10–30 gr. (0·6–2 gm.). It is rather slow in action, produces light normal sleep and is cumulative. It is useless in the presence of severe pain or continuous cough. It is liable to produce headache, faintness, ataxia, coma and delirium, digestive disturbances and hæmatoporphyrinuria. Individuals vary much in their tolerance of sulphonal, large doses of over 200 gr. have been survived, but, on the other hand, medicinal doses may cause toxic symptoms. It is contra-indicated in debilitated, anæmic persons, and is unsuitable for long-continued administration owing to its cumulative action. It is, however, a fairly reliable drug, and has been largely used in spite of its well-known limitations.

Bromural is a crystalline substance with an

odour resembling valerian. It is slightly soluble in cold water, and freely in spirit or hot water. The dose is 5–10 gr. (0·3–0·6 gm.). It acts rapidly (twenty to thirty minutes) and is easily excreted. It is efficient in the same class of case as sulphonal, and is more prompt and reliable in action. Large doses of 60–150 gr. have produced no further effect than prolonged sleep, and the only unpleasant effects recorded after ordinary doses are headache and an irritable rash. As it has not, however, been in use for many years it would be unwise to dogmatise on its safety, or on the minimal toxic dose.

Adalin is a crystalline substance with a slightly acid taste. It is practically insoluble in cold water. The dose is 15 gr. (1 gm.) as a hypnotic. Smaller doses may be efficient in slight cases, and in the more severe an additional ½ gm. (8 gr.) may be necessary. Sleep occurs in about forty-five minutes. It is apparently rapidly excreted, and toxic symptoms are rare after moderate doses. In some cases marked weakness, diarrhœa and delirium have occurred. It has, however, been given without ill-effects in cases of organic and functional cardiac disease, in arteriosclerosis with insomnia, in anæmia, and in many forms of mental and nervous disease. It appears not to be cumulative, but when used over a prolonged period the dose should be gradually diminished. A longer period must elapse before a final judgment on the value of adalin can be pronounced, as the claims made for it have been put forward for other hypnotics when first introduced, and not always maintained after wider experience of their action.

Paraldehyde is a colourless fluid with a peculiarly unpleasant taste and odour. It is fairly soluble in water and mixes well with light alcohol. It is unstable and decomposed by warmth. The dose is ½–2 fl. dr. (2–8 mls.). It is the least powerful of the drugs in this group, and the official maximum doses may, if necessary, be exceeded. The smallest recorded fatal dose is two ounces. It acts rapidly and is very fairly reliable; toxic effects (headache, excitement) are very unusual. To disguise the taste it may be given in strongly sweetened tea, or mixed with pounded ice. Capsules are sold containing 40 minims each, and are probably the best way to give the drug. The patient smells of paraldehyde for some hours. It is diuretic; it may irritate the stomach, so that it should be avoided in cases of gastric disease. A useful combination is 30 minims of paraldehyde with 15 gr. of trional where a rapid and powerful hypnotic effect is required.

Group IV.—Mild Hypnotics

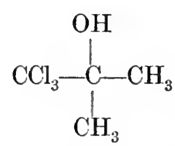
Urethane, a crystalline powder, soluble in water and almost tasteless, is practically only useful for children, who can take 1½ gr. (0·1 gm.) for every year up to fifteen. It acts in twenty to thirty minutes. In smaller doses it may be given per rectum. The adult single dose is 90 gr. (6 gm.). It is apparently excreted as urea.

Hedonal is less soluble and has an unpleasant burning taste. It may be prescribed with spirit and cinnamon water. The dose is 8–15 gr. (0·5 to 1 gm.). Adult males usually require more; as much as 60 gr. (4 gm.) have been given. Sleep occurs in about thirty minutes. It seldom produces toxic effects, but may set up gastro-intestinal irritation. It is not suitable in cases of organic cardiac and vascular disease, but in "simple" insomnia it is efficient and safe.

Amylene hydrate is a colourless liquid, with an unpleasant taste and odour. It is unstable. The dose is 40–70 min. (2–3·5 c.c.), but larger amounts, up to 100 min. (5 c.c.), have been given. It acts rapidly (fifteen to twenty minutes), and this is its great advantage. It is not very reliable and the sleep produced is often short. Gastro-intestinal disturbances are not very infrequent. More serious nervous and circulatory effects are uncommon except after large doses. It is best given in capsules, but the taste may be partially concealed by orange-flower water or liquorice.

Chloral Formamidum, or *Chloralamide*, is a white insoluble powder, and should be given dissolved in an ounce of warm whisky or brandy diluted with water, or with Spiritus Ætheris Nitrosi, which also contains paraldehyde. The dose is 15–45 gr. (1–3 gm.). It only acts after sixty to ninety minutes. In the body chloral and ammonium formate are formed, the latter being a circulatory stimulant. It is the best of the milder hypnotics and may be given in cardiac cases. Its slow action is really its only disadvantage.

Chlorbutol, which is also known by the trade name of *Chloretone*, is chemically trichlorbutyl alcohol—



and has mild hypnotic and antiseptic action. Practically it is not much used as a hypnotic, but it has been recommended as a remedy for chorea, owing to its sedative action. It does not appear to have any uniform superiority over other sedatives in this disease. It has also been rather largely employed as a remedy for sea-sickness, but though good results have been obtained, it is not invariably successful, and may cause a considerable degree of headache. A few cases of tetanus have been recorded in which large doses *per rectum* relieved the spasm and produced sleep. Gastric pains

have been relieved by chlorbutol, but symptomatic treatment of this sort can only be advisable in slighter digestive disturbances, which usually yield to bismuth and other simple remedies. Local applications of 0·4 per cent. solution have been found useful in pruritus vulvæ. Chlorbutol is only slightly soluble in water and has an unpleasant burning taste. It may be given in emulsion with liquid paraffin acacia or tragacanth, but is best administered in cachets, followed by a draught of water. Children of five to ten can take 5 gr. (0·3 gm.) two or three times daily, but the effect must be carefully watched as somewhat alarming stupor may supervene after a few days' continued treatment. For adults the dose is 5–20 gr. (0·3–1·2 gm.), repeated every two or three hours in cases of sea-sickness. *Per rectum* 30 gr. have been given in olive oil.

Preparations

Chloral Hydras (B.P.), *Chloralum Hydratum* (U.S.P.). Colourless crystals with a peculiar nauseous taste and odour. Soluble in water, alcohol, ether and oils. It should not be prescribed in solid form owing to its diliquescent properties.
Dose : 5–20 gr. (3–12 dg.).

Syrupus Chloral (B.P.) contains 10·9 gr. in 1 fl. dr.
Dose : ½–2 fl. dr. (2–8 ml.).

Butyl Chloral Hydras (B.P.). Resembles chloral, but is more nauseous. It has no marked advantages.
Dose : 5–20 gr. (3–12 dg.).

Mistura Butyl-Chloral Hydratis (B.P.C.). Each fluid ounce contains 4½ grains with glycerine and chloroform water.
Dose : ½–1 fl. oz. (15–30 ml.).

Syrupus Butyl-Chloral Hydratis (B.P.C.). Each fluid drachm contains 2 gr. with glycerine, rose-water and syrup.
Dose : 1–4 fl. dr. (4–15 ml.).

Chloral Camphoratum (B.P.C.). Equal parts of chloral hydrate and camphor. A liquid at ordinary temperatures, for rubbing into the skin over neuralgic areas.

Chloral Camphoratum cum Codeina (B.P.C.). Contains 9 parts chloral hydrate, 9 parts camphor, 2 parts cocaine.

Chloral Carbolatum (B.P.C.). Equal parts of chloral hydrate and phenol.

The two last are intended for plugging the cavity of an aching tooth.

Sulphonal (B.P.), *Sulphonmethanum* (U.S.P.). Colourless, tasteless crystals, soluble in hot fluids.
Dose : 10–30 gr. (6–20 dg.).

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Paraldehydum (B.P., U.S.P.). Colourless fluid, with a burning, disagreeable taste and odour.
Dose : 30–120 min. (2–8 ml.). This maximum is often exceeded.

Methyl Sulphonal (B.P.), *Sulphon Ethyl Methanum* (U.S.P.). "Trional," resembles sulphonal, but is more soluble.
Dose : 10–20 gr. (6–12 dg.).

Urethanum (B.P.C.), *Æthylis Carbamas* (U.S.P.). Colourless soluble crystals.
Dose : 15–75 gr. (1–5 gm.).

Barbitonum (B.P.), *Malourea* (B.P.C.). "Veronal" colourless crystals, slightly bitter, soluble in hot water.
Dose : 5–10 gr. (3–6 dg.).

Chloral Formamidum (B.P., U.S.P.), *Chloramidum* (B.P.C.). Chloralamide, colourless crystals, hardly soluble in water, quite soluble in warm dilute spirit.
Dose : 15–45 gr. (1–3 gm.). The maximal dose may be exceeded up to 60 gr.

Mistura Chloramidi Co. (B.P.C.). 30 gr. each of chloramide and potassium bromide in 1 oz., with alcohol and glycerine.
Dose : ½–1 fl. oz. (15–30 ml.).

Bromoformum (B.P.C., U.S.P.). A heavy, colourless liquid; taste and odour resemble chloroform.
Dose : 3 min. (0·2 ml.). As much as 5 min. is sometimes given. An unsatisfactory drug, which were better removed from the pharmacopœia. It is unstable and readily liberates bromine under the influence of light. It does not mix with water, and emulsions are apt to separate so that a large dose remains at the bottom of the bottle and may cause toxic symptoms. Many cases of accidental poisoning have occurred.

The following drugs occur in the B.P.C. only—

Acetophenone (Hypnone).
Dose : 3–8 min. (2–5 dl.).

Benzophenone, diphenyl ketone, a mild hypnotic, mainly used for experimental purposes.
Dose : 3–8 gr. (2–5 dg.).

Glucochloral (Chloralose).
Dose : 3–10 gr. (2–6 dg.).

Homalourea (Proponal).
Dose : 2–6 gr. (1–4 dg.).

Sodium Malourea (Medinal).
Dose : 3–10 gr. (2–6 dg.).

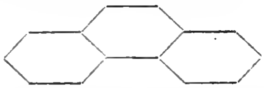
Bromovalerurea (Bromurol).
Dose : 5–10 gr. (3–6 dg.).

Chlorbutol (Chloretone).
Dose : 5–24 gr. (0·3–1·5 gm.).

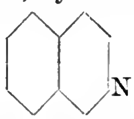
The Alkaloidal Narcotics

Opium and its Derivatives.—Opium, the dried juice expressed from the heads of Papaver

somniferum owes its pharmacological activity to the alkaloids it contains. They are combined with meconic, sulphuric and lactic acids, and are diluted with a number of inactive gums, resins and other bodies. About twenty alkaloids have been isolated from opium; chemically those of which the structure is approximately known belong to one of two groups, those containing a phenanthrene group of three rings (morphine, codeine and thebaine)



and those containing the iso-quinoline group (papaverine, narcotine, narceine, laudosanine, laudanine, cotarnine, hydrocotarnine)



They also present two main physiological actions, a depressant action on the higher cerebral cells, and a convulsant action on the cord, but there is no correspondence between the chemical and physiological groups. The main alkaloids may be arranged as follows, according to their action, beginning with the most depressant and ending with the most convulsant.

Morphine
Papaverine
Codeine
Narcotine
Thebaine
Laudanine.

Therapeutically, the action of opium is mainly dependent on its morphine content; this alkaloid will now be described.

1. *Morphine*.—The effect of a dose of morphine on an animal depends upon the comparative development of the various parts of its nervous system. In man, with his highly developed cerebral hemispheres, it may produce a short stage of excitement followed by depression of the higher cerebral centres. The psychical functions are first depressed, attention, judgment and intellectual processes are weakened, then follows drowsiness, passing into deep sleep with depression of reflexes and marked diminution of sensibility to painful stimuli. There is seldom any exaltation of reflexes or spinal convulsions, such as are seen in some animals. The medullary centres are depressed, especially the respiratory, death occurring from asphyxia. The vasomotor centre and cardiac centre are little affected, but there is slight dilatation of the cutaneous vessels causing mild diaphoresis. The familiar phenomenon of contraction of the pupils is purely a central action; morphine has no effect when applied locally to the eye. The terminal dilatation which occurs in poisoning is due to asphyxia.

The action of the intestines is twofold, and has been thus explained: the splanchnic sympathetic cells are depressed, causing some vasodilatation and increased gastro-intestinal peristalsis from removal of the inhibiting influence. This action is not always observable in man, but is more marked in some animals, causing a fall in blood pressure, diarrhœa and vomiting (Dixon). Subsequently, when the alkaloid is excreted into the stomach and bowel, a local effect is produced on the nerve-endings, peristalsis is checked, and constipation results. Metabolism is decreased, and the secretions generally lessened. There is no perceptible action on the sensory nerve-endings; the effect of hot lead and opium lotion is entirely due to the heat, unless, indeed, some may be ascribed to the patient's knowledge of the supposed anodyne action of the drug.

Morphine is the most powerful narcotic known, and will quiet excitement, kill pain, and produce sleep when all other drugs fail. Its indications are, therefore, very wide. It is not contra-indicated in renal disease, as elimination does not take place by the kidneys, and the urine is unaffected. It must be given with caution in respiratory diseases, as it depresses the centre in the medulla, but is useful in persistent cough where no expectoration is present. Children are very susceptible to its action, and it must, therefore, be given in very small doses and the effect carefully watched, but it is often of great value, even in infancy.

Morphine salts may be given in the following doses: at one month $\frac{1}{1000}$ gr. (0·06 mg.), at three months $\frac{1}{600}$ gr. (0·1 mg.), at one year $\frac{1}{200}$ gr. (0·3 mg.), at five years $\frac{1}{30}$ to $\frac{1}{20}$ gr. (2–3 mg.). As a rule the dose should not be repeated oftener than every two hours. Hypodermic doses should be smaller (Holt).

In glycosuria morphine and codeine are often useful, but must be regarded only as adjuncts to appropriate dietetic treatment.

Morphine may be used to check diarrhœa or induce constipation, but opium is more generally employed for this purpose.

Artificial Derivatives of Morphine

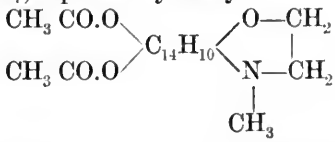
Dionine.—The exact structure of morphine is not absolutely certain. The following formula partially represents its constitution—

$$\begin{matrix} OH \\ OH \end{matrix}\!\!>C_{14}H_{10}\!<\!\begin{matrix} O-CH_2 \\ | \\ N-CH_2 \\ CH_3 \end{matrix}$$

The two hydroxyl (OH) groups differ, in that one resembles that found in alcohol ($C_2H_5.OH$), and the other that in phenol ($C_6H_5.OH$). If the

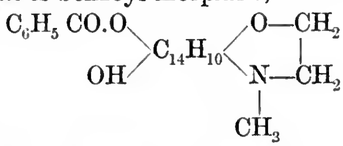
latter is replaced by ethyl (C_2H_5) a body results the hydrochloride of which is soluble in water, and known as dionine. It is rather more powerfully hypnotic than codeine, and, being soluble, may be employed hypodermically. The dose is $\frac{1}{4}$ to $\frac{1}{2}$ gr. (15–30 mg.).

Heroine, or *Diamorphine*, is a diacetic ester of morphine, both the hydrogens of the hydroxyl groups being replaced by acetyl.



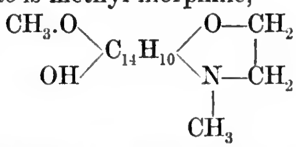
The soporific action is less marked and the convulsant action on the cord more marked than with morphine. It is more depressant on the respiratory centre, and has been mainly used as a sedative for troublesome cough. It is, however, a more dangerous drug than codeine, and not more efficacious. An increase in toxicity has often been observed in a drug when acetyl (CH_3CO) replaces hydroxylic hydrogen (S. Fraenkel). The dose of Heroine, or Diamorphine, hydrochloride is $\frac{1}{25}$ to $\frac{1}{8}$ gr. (2·5–8 mg.).

Peronine is benzoyl morphine,



Its action is similar to codeine, but it is less soluble and has a burning taste. The dose of the hydrochloride is $\frac{1}{8}$ to $\frac{1}{2}$ gr. (8–30 mg.).

2. *Codeine* is methyl morphine,



It has less depressant action on the respiratory centre, is less soporific and less constipating than morphine, but has more convulsant action on the cord. Its main use is to soothe an irritable cough and as a substitute for morphine in diabetes. It is probably the best and safest of all the opium alkaloids for these purposes.

Codeonal is a mixture of sodium veronal (88·24 per cent.) and codeine veronal (11·76 per cent.). It is sold in tablets containing 0·15 gm. of the latter and 0·02 gm. of the former. It is intended for use in cases for which codeine is employed, and has a more marked narcotic action. It may cause abdominal pain and vomiting.

Apomorphine and Apocodeine

These substances may, perhaps, be conveniently described here, although they are not used as hypnotics, and differ both chemically and physiologically from the other derivatives of morphine.

If morphine (under certain conditions) is deprived of the elements of water by a dehydrating agent, a slightly soluble crystalline substance is obtained called apomorphine. The exact chemical structure of this body is not known, but it seems certain that it differs considerably from the parent substance. It is known to contain two hydroxyl groups and a tertiary nitrogen atom (NCH_3). Large doses in animals produce cerebral excitement followed by depression, thus not differing greatly from morphine, but the respiratory centre is markedly stimulated by apomorphine, whereas it is depressed by morphine.

In man, and also in carnivorous mammals, apomorphine stimulates the medullary centres and produces immediate vomiting; this is accompanied by nausea, salivation, increased bronchial secretion and general depression, which are characteristic of the act of emesis, however produced. Experimentally it can be shown that apomorphine acts centrally and not peripherally on the gut, but there is some evidence that, like morphine, some of its effect may be due to paralysis of the sympathetic ganglia which normally inhibit peristalsis.

Apomorphine is a convenient drug when a rapid emesis is required, as it may be administered hypodermically. The indications for its use are, however, somewhat limited, as the passage of a stomach tube is in most cases more effective and safer. The main object of an emetic is to empty the stomach, and this is usually only required where narcotic or irritant poisons have been taken. In narcosis apomorphine does not act well, as the cerebral centres are too depressed to react to medicinal doses, and in irritant poisoning more complete evacuation is assured by the use of a stomach tube and plenty of warm water. In the absence of these simple appliances, however, a hypodermic injection of apomorphine is good treatment. In poisoning by corrosive substances emetics are contra-indicated.

Very small doses may also be employed to increase bronchial secretion and facilitate expectoration. These may be given by the mouth.

In warm-blooded animals death from apomorphine poisoning results from respiratory failure. Collapse occasionally occurs in man after medicinal doses.

Apocodeine can be derived from codeine by dehydration, and its formula is that of codeine less one molecule of water. Its structure is not at present clear; it should theoretically contain one hydroxyl group. It occurs as yellowish grey hygroscopic amorphous powder, freely

soluble in water. Its action resembles that of apomorphine in certain respects, but it does not produce vomiting in man, is more powerfully expectorant and has more marked effect on the sympathetic ganglia, which are inhibited (Dixon). It may, therefore, be employed as a hypodermic purgative, as these ganglia inhibit peristalsis and when paralysed the intestinal movements are increased. It is useless in atony of the muscular walls of the gut.

Solutions of these alkaloidal bodies should be freshly prepared, as they are not very stable.

3. *Narceine* is a very insoluble body, with very little physiological activity. A compound of this alkaloid with sodium salicylate has been introduced as Antispasmin, and is intended as a remedy for whooping-cough. The dose is $\frac{1}{6}$–$1\frac{1}{2}$ gr. (0·01–0·1 gm.). It has not been widely used. Narcyl is the ethyl hydrochloride of narceine, and is similar in its action. The dose is 1 gr. (0·06 gm.).

Opium.—Opium should contain about 10 per cent. of morphine, on which its action largely depends. But there is a prevailing opinion among clinicians that in many cases its action is superior to that of morphine when given in equivalent quantities. The solid drug is more slowly absorbed, and as it remains longer in the intestine it is thought to be more constipating. It is doubtful whether it is less liable to cause nausea.

In order to explain the difference between the action of a given amount of pure morphine and that of the same amount contained in opium, it has been supposed that the other alkaloids, which are present in much smaller amounts, in some way make the morphine more active physiologically, so that the total effect is more than can be accounted for by the mere summation of the narcotic powers of the individual alkaloids present. A similar phenomenon has been stated to occur in the case of the synthetic hypnotics, where a small dose of two dissimilar substances is said to have a greater effect than much larger doses of each given separately. Theoretically, this is expressed by saying that the cerebral cells have different receptors for the various chemical bodies which affect them, and that by giving two such bodies at the same time a larger number of receptors are affected than when only one sort is acted upon. This, of course, is mere speculation, but in accordance with this view several opium substitutes have been prepared which are said to act more powerfully than morphine, and to be thus more valuable in certain conditions.

Pantopon or Omnopon.—This drug was introduced by Sahli and Schärger in 1909, and consists of twenty-one opium alkaloids in the form of hydrochlorides, in the same relative proportions as those in which they occur in opium, as far as this can be determined. It is an amorphous brown powder, easily soluble in water. The solution is stable and faintly acid. The strength of the preparation is said to be five times that of opium, and the dose is $\frac{1}{6}$ to $\frac{1}{3}$ gr. (10–20 mg.). It is usually sold in tablets or in solution (ampoules). It may be used for all purposes for which opium or morphine are prescribed, and has mainly been employed hypodermically with or without scopolamine hydrochloride as an anæsthetic for surgical operations. It is said to have less constipating action than opium or morphine, but otherwise appears to act very similarly.

Narcophine is a mixture of morphine and narcotine in equal parts combined with meconic acid, and four molecules of water. It is a crystalline body easily soluble in water and alcohol, and contains 38 per cent. of morphine. The dose is 15 to 30 drops of a 3 per cent. solution, or $\frac{1}{2}$ gr. (0·03 gm.) subcutaneously. It is said to be more efficacious than morphine alone, and to have less depressant action on the respiratory centre. It is less sedative than codeine in respiratory affections, and apparently acts on the bowel in the same way as morphine.

Toxicology of Opium and its Alkaloids.—Acute poisoning is characterised by somnolence deepening to coma, pin-point pupils, slow respirations, depression of reflexes and occasionally convulsions. The breath may smell of opium. The symptoms closely resemble those of pontine hæmorrhage. The treatment consists in washing out the stomach, preferably with permanganate of potash, the administration of strychnine and caffeine hypodermically, with or without small quantities of atropine, hot coffee per rectum, and cutaneous stimulation with cold towels, sponges, etc. Dr. Frederick Taylor has recently drawn attention to the value of Faradism. When the breathing begins to fail artificial respiration should be persistently employed.

The symptoms of chronic poisoning are not characteristic. Loss of appetite, emaciation and obstinate constipation (though sometimes there may be diarrhœa), and various nervous and mental symptoms occur in pronounced cases. Treatment can only be undertaken in a good nursing home or special institution, and consists usually in the gradual withdrawal of the drug. This requires some six to ten weeks. Relapses are, unfortunately, frequent.

Any opium preparation, as well as the alkaloids morphine and codeine, or the artificial drugs heroine and peronine, may give rise to chronic and habitual excess, the symptoms being much the same whatever particular agent or method is employed.

Preparations

B.P. Preparations.

Opium. The inspissated juice obtained from the unripe capsules of the Papaver somniferum. The dried powder to contain $9\frac{1}{2}$–$10\frac{1}{2}$ per cent. morphine.
Dose: $\frac{1}{2}$–2 gr. (3–12 cg.).

Extractum Opii Siccum. A dry powdered extract standardised to contain 20 per cent. anhydrous morphine.
Dose: $\frac{1}{4}$–1 gr. (15–60 mg.).

Extractum Opii Liquidum. An extract in dilute alcohol, standardised to contain 0·75 per cent. morphine.
Dose: 5–30 min. (3–18 dl.).

Pulv. Opii Co. 10 per cent. opium with pepper, ginger, caraway and tragacanth.
Dose: 5–15 gr. (3–10 dg.).

Pulv. Ipecac. Co. (Dover's powder). 10 per cent. each of opium and ipecacuanha.
Dose: 5–15 gr. (3–10 dg.).

Pulv. Kino Co. 5 per cent. opium, 75 per cent. kino and 20 per cent. cinnamon.
Dose: 5–20 gr. (3–12 dg.).

Pulv. Cretæ Aromaticus cum Opio. $2\frac{1}{2}$ per cent. opium with aromatic chalk powder.
Dose: 10–60 gr. (6–40 dg.).

Pilula Saponis Co. 20 per cent. opium, with hard soap and syrup of glucose.
Dose: 2–4 gr. (12–25 cg.).

Pilula Plumbi cum Opio. 12 per cent. opium, with lead acetate and glucose.
Dose: 2–4 gr. (12–25 cg.).

Pilula Ipecac. cum Scilla. About 5 per cent. opium, Pulv. Ipecac. Co., squills, ammoniacum and glucose.
Dose: 4–8 gr. (25–50 cg.).

Suppositoria Plumbi Co. 1 gr. in each, with lead acetate and oil of theobroma.

Unguentum Gallæ cum Opio. Opium $7\frac{1}{2}$ per cent., with gall ointment.

Tinctura Opii (Laudanum). 1 per cent. anhydrous morphine.
Dose: 5–15 min. (3–10 dl.), for repeated administration 20–30 min. (12–18 dl.) for a single administration.

Tinctura Opii Ammoniata. Nearly 0·5 gr. of opium to the fl. oz. Contains laudanum, benzoic acid, oil of anise and ammonia.
Dose: $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

Tinctura Camphoræ Co. (Paregoric). $\frac{1}{37}$ gr. of anhydrous morphine in 1 fl. dr. Contains laudanum, benzoic acid, camphor, oil of anise and alcohol.
Dose: $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

Linimentum Opii. Contains equal parts of laudanum and soap liniment. It were better omitted from the Pharmacopœia, as laudanum has no local action.

B.P.C. Preparations.

Papaveris Capsulæ (B.P., 1898). The dried fruit of Papaver somniferum, contain a little opium and are intended for use externally as a warm decoction. For this purpose they are quite useless, and hot water fomentations would act equally well.

Acetum Opii (vinegar of opium, black drop). Contains 10 per cent. opium, with nutmeg, sugar, and dilute acetic acid.
Dose: 5–10 min. (3–6 dl.)

Linctus Camphoræ Co. Contains Tinct. Camph. Co. (25 per cent.), with chloroform, syrup of Virginian prune, oxymel of squills, cochineal and senega.
Dose: $\frac{1}{2}$–2 fl. dr. (2–8 ml.).

Linimentum Opii Ammoniatum. Contains Tinct. Opii, 30 per cent., with strong ammonia, and the liniments of ammoniated camphor, belladonna and soap. It is not clear what is the use of the opium in this liniment.

Liquor Opii Sedativus. Contains opium, 10 per cent., with calcium hydroxide, and sherry.
Dose: as Tinct. Opii.

Syrupus Camphoræ Co. Contains Tinct. Opii (1·66 per cent.), camphor, oil of anise, benzoic acid, glacial acetic acid, vinegars of ipecacuanha and squill, sugar, caramel and water.
Dose: $\frac{1}{2}$–1 dr. (2–4 ml.).

Tablettæ Opii. 1 gr. of opium.

Tablettæ Saponis Co. 1 gr. of opium.

Tinctura Opii Crocata (Sydenham's Laudanum). Contains opium (5 per cent.), with cinnamon, cloves, saffron and detannated sherry.
Dose: 10–40 min. (6–24 dl.).

Trochisci Opii. Contain in each $\frac{1}{10}$ gr. of opium in tolu basis.

U.S.P. Preparations.

Opium. Standardised to contain not less than 9 per cent. pure morphine when *moist.*

Extractum Opii. Contains 20 per cent. morphine.
Dose: $\frac{1}{2}$–1 gr. (3–6 cg.).

Opii Pulvis. Standardised to contain 12 per cent. pure morphine.
Average Dose: 1 gr. (65 mg.).

Opium Deodoratum. Opium deprived of the substances soluble in ether. The weight is made up with lactose.
Average Dose: 1 gr. (65 mg.).

Opium Granulatum. A coarse, powdered form.
Average Dose: 1 gr. (65 mg.).

Pulvis Ipecacuanhæ et Opii (Dover's powder). 10 per cent. each of opium and ipecac powder.
Dose: 5–15 gr. (3–10 dg.).

The following U.S.P. fluid preparations contain 10 per cent. morphine, and the dose of each is 5 to 15 min. (3–10 dl.). *Tinctura Opii.* Tinctura Opii Deodorati, Vinum Opii, Acetum Opii (black drops), Tinctura Ipecacuanhæ et Opii.

Tinctura Opii Camphorata (Paregoric) contains 0·4 per cent. opium, with benzoic acid, camphor, oil of anise and glycerine.
Dose: 1–4 fl. dr. (4–15 ml.) for an adult, 5–15 min. (3–10 dl.) for a child.

Mist. Glycyrrhizæ Co. (Brown mixture). Contains 0·05 per cent. opium in the form of Tinctura Opii Camph., with liquorice, syrup, acacia, wine of antimony and spirits of nitrous ether.
Average Dose: 2 fl. dr. (8 ml.).

Pilula Opii. Each contains 1 gr. (0·065 gm.) of opium.

Trochisci Glycyrrhizæ et Opii. Each contains $\frac{1}{12}$ gr. (5 mg.) of opium.

Emplastrum Opii. 6 per cent.

Alkaloids of Opium

B.P. Preparations.

Morphine. The hydrochloride, tartrate and acetate of morphine are the salts usually employed, but the last named were better omitted, as it is unstable. The dose of each is $\frac{1}{8}$–$\frac{1}{2}$ gr. (8–30 mg.). The official solutions (*Liquores*) are all 1 per cent., or 1 gr. in 110 min., of the alkaloidal salt. Their doses are 10–60 min. (6–36 dl.).

From Morphinæ Hydrochloridum are prepared—

Tinctura Chloroformi et Morphinæ Co. 1 per cent., or $\frac{1}{11}$ gr. in 10 min.
Dose: 5–15 min. (3–10 dl.). It contains also tincture of capsicum, tincture of Indian hemp, oil of peppermint, glycerin and alcohol. It is a bad imitation of the proprietary medicine called chlorodyne.

Trochiscus Morphinæ. $\frac{1}{32}$ gr. in tolu basis.

Trochiscus Morphinæ et Ipecac. $\frac{1}{32}$ gr. with ipecacuanha in tolu basis.

Suppositoria Morphinæ. $\frac{1}{4}$ gr. in oil of theobroma.

From Morphinæ Tartras is prepared—

Injectio Morphinæ Hypodermica. Contains 2·5 per cent., or 1 gr. in 44 min.
Dose: 5–10 min. subcutaneously (3–6 dl.).

B.P.C. Preparations.

Oleinatum Morphinæ. 1 in 50 for application to skin.

Pastillus Morphinæ. $\frac{1}{30}$ gr.

Linctus Sedativus. Contains $\frac{1}{32}$ gr. morphine hydrochloride to the drachm, with lemon juice, chloroform and glycerine.
Dose: $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

Trochisci Morphinæ et Ipecac. Compressæ. Each contains $\frac{1}{36}$ gr. morphine hydrochloride.

Injectio Morphinæ et Atropinæ Hypodermicæ. Contains $\frac{1}{2}$ gr. morphine tartrate and $\frac{1}{100}$ gr. atropine sulphate in 8 min.
Dose: 2–8 min. (1–5 dl.).

U.S.P. Preparations.

The pure *alkaloid*, the *sulphate*, the *hydrochloride* and the *acetate* are official. The last named is unstable. The dose of each is $\frac{1}{12}$ – $\frac{1}{2}$ gr. (5–30 mg.).

Pulvis Morphinæ Co. Contains morphine sulphate, about 1·5 per cent., with liquorice powder and camphor.
Dose: 5–15 gr. (3–10 dg.).

Codeine. The alkaloid and its phosphate are official in the B.P. The sulphate is official also in the U.S.P. The dose of each is $\frac{1}{4}$–1 gr. (16–60 mg.), and the Hydrochloride in the B.P.C.

Syrupus Codeinæ Phosphatis (B.P.). Contains 0·27 gr. codeine phosphate in 1 fl. dr.
Dose: $\frac{1}{2}$–2 fl. dr. (2–8 ml.).

Linctus Codeinæ (B.P.C.). Is similar, but only half as strong.
Dose: $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

Gelatinum Codeinæ (B.P.C.). Contains 1 in 500 of the alkaloid.
Dose: 60 gr. (4 g.).

Pastillus Codeinæ (B.P.C.). Contains $\frac{1}{8}$ gr. of the alkaloid.

Diamorphinæ Hydrochloridum (B.P.). Acetomorphinæ Hydrochloridum (Heroine).
Dose: $\frac{1}{25}$ – $\frac{1}{8}$ gr. (2·5–8 mgm.).

Elixir Acetomorphinæ et Terpini (B.P.C.). Containing $\frac{1}{18}$ gr. in 1 fl. dr.
Dose: $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

Linctus Acetomorphinæ (B.P.C.). $\frac{1}{18}$ gr. in 1 fl. dr.
Dose: $\frac{1}{2}$–2 fl. dr. (2–8 ml.).

Pastillus Acetomorphinæ (B.P.C.).
Containing $\frac{1}{20}$ gr.

Trochisci Acetomorphinæ (B.P.C.).
Containing $\frac{1}{20}$ gr.

Pastillus Acetomorphinæ Co. (B.P.C.).
Containing $\frac{1}{32}$ gr.

Elixir Acetomorphinæ et Pini Co. (B.P.C.). $\frac{1}{30}$ gr. in 1 fl. dr.
Dose: $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

Glycerinum Acetomorphinæ (B.P.C.). $\frac{1}{36}$ gr. in 1 fl. dr.
Dose: $\frac{1}{2}$–2 fl. dr. (2–8 ml.).

Pastillus Acetomorphinæ et Terpini (B.P.C.).
Containing $\frac{1}{40}$ gr.
Pastillus Acetomorphinæ et Pini Co. (B.P.C.).
Containing $\frac{1}{48}$ gr.
Pastillus Acetomorphinæ et Terpini et Mentholis (B.P.C.).
Containing $\frac{1}{400}$ gr.
Apomorphinæ Hydrochloridum (B.P., U.S.P.).
Dose: $\frac{1}{20}-\frac{1}{10}$ gr. (3–6 mg.). If given by the mouth a dose up to $\frac{1}{4}$ gr. (15 mg.) may be given.
Injectio Apomorphinæ Hypodermica (B.P.). 1 per cent. solution.
Dose: 5–10 min. 3–6 dl.).
Pastillæ Apomorphinæ et Codeinæ (B.P.C.), contain apomorphine hydrochloride $\frac{1}{30}$ gr., and codeine $\frac{1}{10}$ gr. in each. Sedative expectorant.
Syrupus Apomorphinæ (B.P.C.) contains about $\frac{1}{32}$ gr. in each fluid drachm.
Dose: $\frac{1}{2}$–1 fl. dr. (2–4 ml.).
Tabellæ Apomorphinæ (B.P.C.). Chocolate, containing 2 mg. ($\frac{1}{32}$ gr.) of the hydrochloride in each.

Cannabis Indica.—This drug consists of the flowering tops of the female plant of Indian Hemp, *Cannabis sativa;* from its oleoresin can be extracted *cannabinol*, which is the active principle. Small amounts of ammonium bases allied to choline are also present. The drug and all its preparations vary much in their physiological activity, and cannabinol itself, an aldehyde, is unstable. The action on the brain appears to resemble that of opium, but is accompanied by more restlessness in the earlier stages, and is credited with producing dreams and hallucinations of a captivating character. There is marked analgesia. There is no disturbance of digestion. There is some paretic effect on the muscles, slight diuresis, and but little action on the respiration. Death occurs from cardiac failure. It is not a good drug, as the strength of the preparations varies considerably and the active principle is unstable. It may, however, be tried as a substitute for opium where that drug is contra-indicated. It is sometimes given for neuralgia, migraine and dysmenorrhœa. There is some reason for the view that the effects of the oriental preparations of Cannabis are due to the other ingredients of the complex form in which it is taken.[1]

Lactucarium, the dried juice of common lettuce, contains bitter principles, said to have hypnotic action. It is practically valueless.

Lupulus, the dried strobiles of hops, contains lupumaric acid, a volatile oil and traces of other bodies. They have a mild hypnotic action. "Hop pillows," once a favourite remedy for insomnia, probably owed their efficacy to mental impressions rather than physiological activity.

[1] Ball, *Therapeut. Gazette*, Vol. XXXIV. p. 77 (1910).

Official Preparations

Cannabis Indica (B.P., U.S.P.). Flowering tops of the female plant Cannabis sativa, grown in the East Indies.
Extractum Cannabis Indicæ (B.P., U.S.P.).
Dose: $\frac{1}{4}$–1 gr. (15–60 mg.).
Tinctura Cannabis Indicæ (B.P.).
Dose: 5–15 min. (3–10 dl.).
Fluidextractum Cannabis Indicæ (U.S.P.).
Average Dose: 1 min. (5 cl.).
Lactucarium (U.S.P.). The dried juice of Lactuca virosa, the common lettuce.
Dose: 5–15 gr. (3–10 dg.).
Tinctura Lactucariæ (U.S.P.).
Dose: 15–30 min. (1–2 ml.).
Syrupus Lactucariæ (U.S.P.).
Dose: 2 fl. dr. (8 ml.).
Lupulus.
Humulus (U.S.P.).
Infusum Lupuli.
Dose: 1–2 fl. oz. (30–60 ml.).
Tinctura Lupuli (alcoholic).
Dose: $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

J. M. F.-B.

VEGETABLE ASTRINGENTS

The vegetable astringents all contain a considerable proportion of tannic acid, and to this body, which is widely distributed in the plant kingdom, their actions are due. Pure tannic acid is an anhydrous monobasic acid ($C_{13}H_9O_7.COOH$) obtained from the oak gall. The various tannins are by no means identical chemically, although their pharmacological properties remain similar; thus a large number of physiological plant tannins are glucosides which, on hydrolysis, yield sugar or phloroglucin (*e. g.* kino-tannic acid), and various complex acids of the phenol series, such as gallic acid, coffeic acid, etc., or phlobaphenes, coloured resinous bodies, such as rhatany-red, china-red; other tannins derived from pathological plant growths, *e. g.* oak galls, are compounds of two molecules of gallic acid, $(OH)_3C_6H_2.COOH$ with the loss of one molecule of water, *i. e.* digallic acids, such as is pure tannic acid. They are derivatives of the trihydroxy-benzoic acids, and are thus chemically allied to salicylic acid (mono-hydroxy-benzoic acid).

The value of tannic acid in the arts and in pharmacology depends largely on its chemical reactions. It is soluble in water, alcohol and glycerin, and solutions form with albumen or gelatin dense precipitates of tannate of albumen or gelatin, which are soluble in excess of the latter or in acids and alkalies. It possesses the power of converting connective tissue into leather, which, unlike the former, does not swell up and decompose in the presence of moisture. Tannic acid is precipitated by mineral acids

and itself precipitates tannates with heavy metallic salts and alkaloids and certain glucosides. The alkaloidal tannates are white in colour and usually redissolve on the addition of a dilute organic acid, *e. g.* acetic, or of alcohol. Tannic acid is employed as a group test for alkaloids. With neutral solutions of ferrous salts tannic acid gives a purple-black colour, if free acid is present no colour appears; with ferric salts, a green to blue-black colour is produced which is utilised in the formation of inks; gallic acid with ferrous salts forms a blue-black ink.

Pharmacology.—The principal action of the tannic acid series is that of astringency—the property of diminishing the amount of secretion from living tissues. This action depends on the power of tannic acid to precipitate albuminous materials. This power is inherent in the acid radicle, and if this be neutralised either by an alkali or by albumen the astringent property is lost. When tannic acid is applied to a mucous surface the proteins in the superficial cells are precipitated; this forms a protective coating over the surface, the precipitation of the cell proteins checks their secretions, and at the same time limits the growth of the cells. Direct application of tannic acid to blood vessels, if the solution be weak, causes slight constriction; stronger solutions cause a transitory constriction followed by dilatation. The value of the drug in hæmorrhage is due largely to its rapid precipitation of the blood proteins, which later coagulate. At the same time, however, tannic acid, locally applied, may indirectly limit and diminish the size of the arterioles and capillaries, by the protein precipitation in the surrounding cells forming a more resistant bed for the vessels. While this is the property of tannic acid, it is possessed in no degree by gallic acid, which has no power of precipitating proteins and therefore no astringency.

External.—Tannic acid has decided antiseptic properties, partially of a specific nature, like others of its related chemical compounds, but largely from its power of precipitating albumen. Its antiseptic action is overshadowed by its astringency, although it is important to note that the layer of coagulated proteins it produces does not readily become septic. When applied to a raw surface, tannic acid precipitates the superficial proteins which form a protective coating for the tissues beneath, the secretion of the cells is checked, and, should inflammation be proceeding, the lumen of the capillaries is indirectly diminished, rendering the tissues paler, and any diapedesis of leucocytes which has been in progress is retarded and finally stopped. Stronger solutions of tannic acid act in the same way as styptics, and concentrated solutions are actually caustic by causing death of the cells. Tannic acid solutions also check excessive secretion of the sweat glands and harden the integument.

Internal. (1) *Mouth.*—When applied to mucous surfaces such as that of the mouth, nose or throat, etc., a sensation of dryness, roughness and constriction of the tissues is experienced, due to the specific astringent action of tannic acid. Secretion is also limited and a feeling of thirst ensues.

(2) *Stomach.*—Reaching the stomach, tannic acid precipitates the albuminous materials in the food in the form of tannates; these are later redigested, the albumen to peptone—which is not precipitated by tannic acid—and therefore the acid is again liberated. Large doses of tannic acid, purely by precipitating the albumen in the food, may cause symptoms of indigestion. In neutral solutions tannic acid precipitates pepsin, but this is unlikely to occur in the stomach unless in conditions of achlorhydria. So long as the tannic acid remains in combination with albumen its astringency is absent, but when it is in the free state, the astringent action is exerted on the mucous membrane of the stomach walls and diminishes their secretions. It will also restrain hæmorrhage from the walls of the stomach. In general, therefore, tannic acid interferes with the process of gastric digestion, and, when large doses have been given or where the stomach is empty, the astringent effect on the stomach walls may give rise to definite irritation and cause vomiting.

(3) *Intestine.*—The astringent effect persists for some time in the small intestine, the mucous and glandular secretions are lessened, and the precipitation of proteins in the superficial layers of the bowel forms a protective coating, allaying irritation and reflexly diminishing peristaltic movements. Thus the contents of the bowel are delayed in transmission and more time is allowed for the absorption of the watery portion of the intestinal contents; the result of these factors is the checking of diarrhœa and an increase in the consistency of the stools. As in the stomach, large doses give rise to irritant symptoms and often cause diarrhœa. In the intestine tannic acid exerts its mild antiseptic action and by precipitating the proteins of putrefactive organisms causes their death; this action, however, is not powerful and cannot be relied upon to any great degree. Tannic acid is decomposed in the bowel to form gallic acid, and this, together with the parent substance, unite with alkali to form sodium gallate or tannate. Tannates and gallates have no astringent powers, and therefore the astringent action is limited to the upper part of the intestine. As will be mentioned under therapeutics, drugs have been prepared to avoid this rapid loss of action.

It has just been stated that tannic acid is converted in the intestines to gallic acid; part of

it is absorbed in the form of alkaline gallates, and carried through the blood to be excreted in the urine; a very small proportion may be absorbed as alkaline tannates while another portion is excreted as gallates in the fæces. The greater part of the tannic acid administered by mouth cannot be recovered since it undergoes complete oxidation and thus disappears. Occasionally the gallic acid excreted in the urine forms pyrogallic acid on standing, and the urine assumes a darker tint.

(4) *Actions after Absorption.*—Since neither alkaline tannates nor gallates exert any astringent action, tannic acid can possess no astringent properties after absorption; in the circulation, therefore, it causes no constriction of the arteries and no rise in blood pressure. Tannic and gallic acids have long been considered as remote astringents and styptics, but there is absolutely no evidence of their value as such. No remote disinfectant action on the urinary system is exerted by them, and the assertion that they diminish albuminuria in Bright's disease is now wholly discredited.

Therapeutics. External.—For external treatment pure tannic acid is used much more frequently than the vegetable drugs containing it. It is applied locally to wounds, ulcers and bleeding surfaces, in the form of dusting powders, ointments, 10 per cent. (60 gr. in 1 oz.), or lotions, 2–5 per cent. (10–20 gr. in 1 fl. oz.), which may be employed to impregnate lint or cotton wool. It is particularly useful in those cases where excessive secretion is present as in weeping ulcers and chronic or subacute inflammatory conditions. From its action in hardening the skin it is occasionally useful as an application for the prevention of bedsores and blisters, and is of value, either as a dusting powder or in the form of the glycerin, for checking excessive local perspiration and reducing the discharge in intertrigo and other skin diseases. Injections or bougies containing tannic acid are frequently employed for the treatment of inflammatory discharges from the urethra and vagina, *e. g.* urethritis and leucorrhœa, while in the form of ointments such as the Unguentum Gallæ or as the suppository it is of great benefit in the palliative treatment of hæmorrhoids. The opium in Unguentum Gallæ cum Opio is useless as a local anodyne, since opium is purely central in action; it may be replaced by cocaine. The Glycerinum Acidi Tannici is useful as a hardening agent in sore and inflamed nipples, directions being given for it to be washed off before giving the child the breast. Weak solutions or the powder are of value in checking excessive discharge in otorrhœa.

Internal. (1) *Mouth.*—Tannic acid is a very valuable astringent in cases of swollen and tender gums which readily bleed. Tonsillitis and inflammatory conditions of the fauces and uvula are amenable to treatment by it, and relaxed sore-throat, pharyngitis and laryngitis are curable by its exhibition. For the former cases, mouth washes or gargles of tannic acid, 2 per cent. (10 gr. in 1 fl. oz.), or of the Glycerinum, 10 per cent. (1 fl. dr. in 1 fl. oz.), or lozenges may be used; sprays of the same strength are also valuable. The constringent effect of gargles in the mouth will, however, alone prevent the acid coming into intimate contact with the tonsils, etc., and, in such cases and for pharyngitis and laryngitis, paints of the Glycerinum are best employed; a useful paint is a mixture of equal quantities of the Glycerinum with Glycerinum Aluminis. A strong solution of tannic acid in spirit has been advised in pyorrhœa alveolaris, but the treatment is merely temporary and palliative, and should be employed only after suitable surgical and vaccine treatment has been undergone. In nasal catarrh and epistaxis, douches, 0·5 per cent. (3 gr. to 1 fl. oz.), and snuffs, containing tannic acid, are of great value in checking secretion or hæmorrhage, and occasionally dilute solutions are employed in conjunctivitis.

(2) *Stomach.*—The astringent effects of pure tannic acid in the stomach are somewhat powerful, and it is advisable, therefore, to adopt for internal administration some of the vegetable astringents in which the tannic acid is to a greater or less degree enclosed in cells or surrounded by colloid materials, which considerably delay its passage into solution or its activity in combining with protein substances and causing irritant symptoms. With these reservations the vegetable astringents are useful in chronic catarrhal gastritis and in certain forms of dyspepsia by limiting the secretion of the glands; for this purpose the Pulvis Catechu Compositus is a particularly suitable preparation. When hæmorrhage is occurring from the stomach, *e. g.* from a gastric ulcer, tannic acid may be employed; but some of the metallic astringents, such as bismuth, having a more sedative action, are preferable. Tannic acid is, however, of importance as an antidote in cases of poisoning from alkaloids and heavy metallic salts; large quantities should be given in dilute solution, and followed by an emetic and purge.

(3) *Intestine.*—Tannic acid and the drugs containing it exert their astringent effect in the small intestine until they are neutralised or decomposed. Naturally the process is slower in the case of the vegetable astringents, especially when given in powder or pilular form, and they are therefore of greater advantage in the treatment of intestinal conditions. Their effects are important in the treatment of diarrhœa in its various forms, particularly where this is due to inflammatory processes of a subacute or chronic nature characterised by increased mucous secretion. For this purpose tannic acid

and the vegetable astringents are suitably prescribed along with chalk, bismuth or opium. Where the diarrhœa is caused by putrefactive or fermentative processes the antiseptic action of the tannic acid may be of some service, but in view of its mild character the action of the astringent is best supplemented by that of an intestinal antiseptic.

In intestinal hæmorrhage from ulcer tannic acid is often of service administered in the form of catechu, kino, or krameria combined with opium as a sedative. Since tannic acid is rapidly converted into non-astringent gallic acid it has no local action on the large intestine when administered by mouth; hence enemata have been employed for the treatment of mucous colitis, cholera and dysentery. Where the catarrhal condition is confined to the rectum the suppository may be of advantage.

In view of the fact that tannic acid is rapidly decomposed, and rendered inert in the intestine, various preparations have been evolved which shall preserve the astringency in the lower bowel. These preparations are synthesised mainly on the principle of forming a compound which shall be insoluble in the stomach—and therefore free from irritant properties—but which shall liberate its tannic acid in the alkaline contents of the intestine. Tannalbin, a compound of albumen and tannin, *Dose* 8–15 gr. (5–10 dg.), is a pale brown, insoluble, tasteless powder, containing 50 per cent. tannic acid. It is not affected by the action of the gastric juice and remains inactive till digested in the intestine. Even in this compound, however, the tannic acid undergoes complete conversion into gallic acid before excretion in the fæces. Tannigen, diacetyl-tannin $C_{24}H_8(COCH_3)_2O_9$, *Dose* 5–15 gr. (3–10 dg.), is a tasteless, insoluble powder, soluble in alkalies. The large proportion of this compound is also converted into gallic acid and absorbed, but a small part is excreted in the fæces. Tannoform, methylditannin, $C_{29}H_{20}O_{18}$, *Dose* 1–20 gr. (1–12 dg.), a compound of tannic acid and formaldehyde, insoluble in water but soluble in alkalies, is employed both as an intestinal astringent and as a local astringent for raw surfaces. Tanocol, *Dose* 10–15 gr. (6–10 dg.), is a compound of tannic acid and gelatin; it is a white, tasteless, insoluble powder. Honthin, albumen tannate, *Dose* 10–30 gr. (6–20 dg.), is insoluble in water, but is separated into its components in the gastric juice. Glutanol, a combination of tannic acid and vegetable fibrin, *Dose* 5–15 gr. (3–10 dg.), is similar in action to tannalbin. Tannone, a compound of tannic acid and hexamethylene-tetramine, *Dose* 5–15 gr. (3–10 dg.), or tannopin is not so powerfully antiseptic as tannoform. Other tannic acid compounds are tannothymol, tannal and tannocase.

(4) *Remote Therapeutics.*—As has already been explained under the head of pharmacology, tannic acid is of no value after absorption. It has been given in Bright's disease to diminish albuminuria and to check bleeding from the lungs, kidney and uterus. There is absolutely no ground for believing the drug to be of any value in such cases; the same statement applies with equal force to the employment of gallic acid as a remote astringent in phthisis.

Preparations

Acidum Tannicum (B.P., U.S.P.).
$C_{13}H_9O_7.COOH$. Characters, light brownish powder with astringent taste, soluble in water, alcohol and glycerin.
Dose : 5–10 gr. (3–6 dg.).
(*a*) Glycerinum Acidi Tannici (B.P., U.S.P.). 20 per cent. in glycerin.
(*b*) Trochiscus Acidi Tannici (B.P., U.S.P.). ½ gr. (0·03 g.).
(*c*) Suppositoria Acidi Tannici (B.P.). 3 gr. (0·2 g.).
(*d*) Gargarisma Acidi Tannici (B.P.C.). 1 to 9 of water.
(*e*) Collodium Stypticum (U.S.P.). Tannic acid 20, alcohol 5, ether 25, collodium to 100.
(*f*) Unguentum Acidi Tannici (U.S.P.). 1 to 4.

Acidum Gallicum (U.S.P.). $C_6H_2(OH)_3COOH$. Characters, colourless or yellowish silky needles, soluble in water, alcohol and glycerin.
Dose : 5–15 gr. (3–10 dg.).
(*a*) Dermatol, Bismuth sub-gallate (U.S.P.).
Dose : 10–30 gr. (6–20 dg.).
(*b*) Airol, Airoform, Airogen, Bismuth oxy-iodo-gallate (B.P.C.).
(*c*) Gallanol. Gallic acid anilide, used in psoriasis and eczema.
(*d*) Galloformin. A compound of gallic acid and hexamethylene-tetramine, is an external disinfectant.
(*e*) Gallobromol. Dibromo-gallic acid. A substitute for bromides and as injection in gonorrhœa (1 per cent.).
Dose : 8–15 gr. (5–10 dg.).

Galla (B.P., U.S.P.). Excrescences on the twigs of Quercus infectoria, Asia Minor, produced by the deposition of eggs of the gall saw-fly, Cynips Gallæ tinctoriæ. Characters, hard, sub-globular, tuberculated, nut-like bodies of a dark olive green colour. Active principle—Gallo-tannic acid.
(*a*) Unguentum Gallæ (B.P., U.S.P.). 20 per cent.
(*b*) Unguentum Gallæ cum Opio (B.P.) Contains 7½ per cent. of Opium. N.B.—Opium has no local action in relieving pain, hence cocaine should be substituted.

(c) Decoctum Gallæ (B.P.C.).
(d) Tinctura Gallae (U.S.P.).
Dose : 1–3 fl. dr. (4–12 ml.).

Catechu (B.P., U.S.P.). An extract of the leaves and young shoots of Uncaria Gambier, Malay Archipelago. Characters, light cubes, dark brown externally, light brown internally. Active principle. Catechu-tannic acid $C_{36}H_{34}O_{15}$.
Dose : 5–15 gr. (3–10 dg.).
(a) Pulvis Catechu Compositus (B.P.). Contains catechu, kino, krameria, cinnamon, nutmeg.
Dose : 10–60 gr. (6–40 dg.).
(b) Tinctura Catechu (B.P.). Tinctura Gambir Composita (U.S.P.).
Dose : ½–1 fl. dr. (2–4 ml.).
(c) Trochiscus Catechu (B.P.). 1 gr. (0·06 g.) in each. Trochiscus Gambir (U.S.P.).
(d) Mistura Catechu et Cretæ. Tincture of catechu with chalk mixture.
Dose : ½–1 fl. oz. (15–30 ml.).

Catechu Nigrum (B.P.). An extract of the heartwood of Acacia Catechu, India.
Dose : 5–15 gr. (3–10 dg.).

Krameria Radix (B.P., U.S.P.). Rhatany root obtained from Krameria triandra or Krameria argentea, Peru and Pará. Characters, cylindrical, dark reddish-brown root, taste astringent, colours saliva red. Active principle, rhatania-tannic acid, $C_{54}H_{24}O_{21}$.
Dose : 15–60 gr. (1–4 g.).
(a) Extractum Krameriæ (B.P., U.S.P.).
Dose : 5–15 gr. (3–10 dg.).
(b) Fluidextractum Krameriæ (U.S.P.).
Dose : 15 min. (1 ml.).
(c) Infusum Krameriæ (B.P.). Infusum Krameriæ Concentratum (B.P.C.) is seven times stronger.
Dose : ½–1 fl. oz. (15–30 ml.).
(d) Tinctura Krameriæ (B.P., U.S.P.).
Dose : ½–1 fl. dr. (2–4 ml.).
(e) Trochiscus Krameriæ (B.P., U.S.P.). 1 gr. (0·06 g.) of Extract in each.
(f) Trochiscus Krameriæ et Cocainæ (B.P.). Extractum Krameriæ 1 gr. (0·06 g.), cocaine hydrochloride $\frac{1}{20}$ gr. (0·003 g.) in each.
(g) Gargarisma Krameriæ (B.P.C.).
(h) Syrupus Krameriæ (U.S.P.).
Dose : 1–2 fl. dr. (4–8 ml.).

Hæmatoxyli Lignum (B.P., U.S.P.). Logwood, the heartwood of Hæmatoxylon campechianum, Central America and West Indies. Characters, dull orange-red chips, with astringent taste, colours saliva pink. Active principles, tannic acid and hæmatoxylin.
(a) Decoctum Hæmatoxyli (B.P.).
Dose : ½–2 fl. oz. (15–60 ml.).
(b) Extractum Hæmatoxyli (U.S.P.).
Dose : 10–30 gr. (6–20 dg.).
(c) Extractum Hæmatoxyli Liquidum (B.P.C.).
Dose : ½–2 fl. dr. (2–8 ml.).
(d) Mistura Hæmatoxyli cum Catechu (B.P.C.). Contains tincture of catechu, aromatic sulphuric acid, and decoction of logwood.
Dose : ½–1 fl. oz. (15–30 ml.).

Sappan (B.P.). The heart wood of Cæsalpinia Sappan. Active principles, tannic acid and colouring matters.
(a) Decoctum Sappan (B.P.).
Dose : ½–2 fl. oz. (15–50 ml.).

Kino (B.P., U.S.P.). The dried juice from the trunk of Pterocarpus Marsupium, South India and Ceylon. Characters, small angular, dark red or almost black fragments, taste astringent, tinge saliva red. Active principle, kino-tannic acid, $C_{18}H_{18}O_8$.
Dose : 5–20 gr. (3–12 dg.).
(a) Pulvis Kino Compositus (B.P.). Contains 5 per cent. of opium with cinnamon.
Dose : 5–20 gr. (3–12 dg.).
(b) Tinctura Kino (B.P., U.S.P.).
Dose : ½–1 fl. dr. (2–4 ml.).
(c) Trochisci Kino (B.P.C.). 2 gr. (12 cg.) in each.

Kino Eucalypti (B.P.). Botany Bay Kino, an exudate from the stems of Australian species of Eucalyptus. Characters, irregular dark red pieces. Active principle, kino-tannic acid.
Dose : 5–20 gr. (3–12 dg.).
(a) Trochiscus Kino Eucalypti (B.P.). 1 gr. (0·06 g.) in each.

Buteæ Gummi (B.P.) Bengal Kino. The inspissated juice from the stem of Butea frondosa. Characters, shining, ruby-coloured fragments. Used to make official preparations of Kino in India and Eastern Colonies.

Eucalypti Gummi (B.P., 1898). An exudate from the bark of Eucalyptus rostrata, Australia. Characters, small reddish opaque fragments adhering to the teeth and colouring saliva red. Active principle, kino-tannic acid.
Dose : 2–5 gr. (12–30 cg.).
(a) Trochiscus Eucalypti Gummi (B.P., 1898). 1 gr. (0·06 g.) in each.
(b) Extractum Eucalypti Gummi Liquidum (B.P.C.).
Dose : 30–60 min. (2–4 ml.).
(c) Gargarisma Eucalypti Gummi (B.P.C.). 1 of extract in 16.
(d) Syrupus Eucalypti Compositus (B.P.C.). Contains oil of eucalyptus.
Dose : ½–1 fl. dr. (2–4 ml.).
(e) Tinctura Eucalypti Gummi (B.P.C.).
Dose : 15–40 min. (1–2·5 ml.).

Hamamelidis Cortex (B.P., U.S.P.). The bark of Hamamelis virginiana, North America. Characters, thin, channelled, reddish-brown pieces. Active principle, crystalline hamamelitannin, and amorphous tannic acid.

Dose : 15–45 gr. (1–3 g.).

(*a*) Tinctura Hamamelidis (B.P.).
Dose : $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

(*b*) Aqua Hamamelidis (U.S.P.).
Dose : 2 fl. dr. (8 ml.).

Hamamelidis Folia (B.P., U.S.P.). The leaves of Hamamelis virginiana, North America. Characters, oval leaves, 7–15 cm. long with obtuse apex and sinuate margin. Active principle, tannic acid.

Dose : 15–45 gr. (1–3 g.).

(*a*) Extractum Hamamelidis Liquidum (B.P., U.S.P.).
Dose : 5–15 min. (3–10 dl.).

(*b*) Liquor Hamamelidis (B.P.).
Dose : 1–3 fl. dr. (4–12 ml.).

(*c*) Unguentum Hamamelidis (B.P.). 10 per cent. of liquid extract.

(*d*) Pasta Hamamelidis (B.P.C.). Witch Hazel Snow. 1 per cent. of liquor in 2.

(*e*) Hamamelinum (B.P.C.).
Dose : 1–5 gr. (6–30 cg.).

(*f*) Suppositoria Hamamelini et Zinci Oxidi (B.P.C.).

Belæ Fructus (B.P.). The half-ripe fruit of Aegle Marmelos, India. Characters, spherical or ovoid berry, 7–8 cm. in diameter. Active principle, tannic acid.

(*a*) Extractum Belæ Liquidum (B.P.).
Dose : 1–2 fl. dr. (4–8 ml.).

Acaciæ Cortex (B.P.). The dried bark of Acacia arabica and Acacia decurrens.

(*a*) Decoctum Acaciæ Corticis (B.P.).
Dose : $\frac{1}{2}$–2 fl. oz. (15–60 ml.).

Myrobalanum (B.P.). The dried immature fruits of Terminalia Chebula.

Dose : 30–60 gr. (2–4 g.).

(*a*) Unguentum Myrobalani (B.P.). 20 per cent.

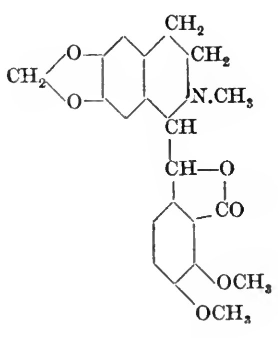
(*b*) Unguentum Myrobalani cum Opio (B.P.). Contains 7·5 per cent. of Opium.

W. J. D.

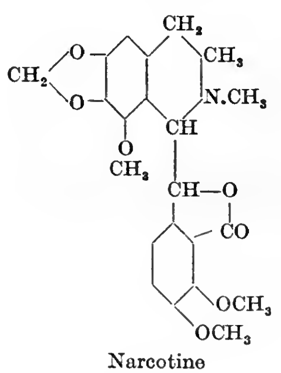
THE HYDRASTIS GROUP OF ALKALOIDS

Hydrastis Canadensis, the golden seal, owes the greater part of its activity to the presence of the isoquinoline alkaloid, *Hydrastine*, though *Berberine* and *Canadine* are also present.

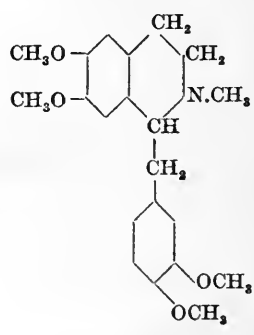
Hydrastine has close chemical and pharmacological relationships with the minor opium alkaloids, as for example narcotine and laudanosine—



Hydrastine

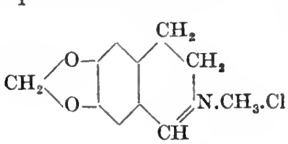


Narcotine

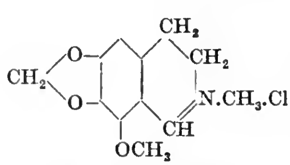


Laudanosine

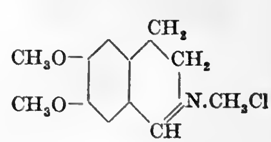
These three alkaloids are readily converted by oxidative decomposition into more simple isoquinoline alkaloids—



Hydrastinine chloride



Cotarnine chloride



6:7-dimethoxy-2-methyl-3:4 di-hydro*iso*quinolinium chloride.

These derivatives have again very similar pharmacological properties and will be considered later.

The most characteristic action of hydrastine is its effect upon the central nervous system. In the frog, after a short period of depression, reflexes become greatly exaggerated and typical strychnine-like convulsions develop. In the mammal similar symptoms are met with, but much larger doses are necessary to produce any increase in reflex excitability, and very large doses are required to produce convulsions. The convulsions are due to increased excitability of the spinal cord, and the effects are very similar to those produced by narcotine, thebaine, etc. The medulla is also stimulated. The heart is slowed, the respiration is quickened and deepened, and the blood pressure is raised, through stimulation of the respective centres. When sufficient of the alkaloid has been given to produce convulsions death usually occurs, from respiratory failure, during a tetanic spasm.

On the circulation the effect produced is the resultant of conflicting factors. Stimulation of the vasomotor centre tends to raise the blood pressure, but the cardiac inhibition acts in the opposite direction. By a direct action on the heart muscle the heart is weakened and the output somewhat diminished. Hydrastine has no direct constrictor influence on the plain muscle of the arterioles. If the vessels be cut off from the vasomotor centre by section of the cord in the neck, a fall of blood pressure follows an injection of hydrastine. Some observers find, indeed, that a fall of blood pressure is the usual result in the normal animal, the stimulating effect on the vasomotor centre being insufficient to counteract the cardiac depression and inhibition induced by the alkaloid. Small rises of pressure have been observed by others. Very large doses paralyse the vagus inhibitor fibres and have a very depressant influence on the heart muscle.

The intestinal movements are increased by hydrastis preparations, but it is probable that canadine and berberine are responsible for most of this effect. Some observers have found that hydrastine causes uterine contractions; others have failed to confirm this observation; clinical evidence, however, indicates that hydrastine has a stimulating action on uterine muscle. In this respect, as also in blood-pressure-raising properties, hydrastine is inferior to the simpler isoquinoline alkaloids hydrastinine and its allies. It is thus less frequently employed than it used to be.

Hydrastine is not oxidised in the body, but is excreted unchanged.

The presence of *Berberine* in hydrastis imparts a bitter flavour to its preparations (see *Simple Bitters*). Apart from this berberine has little action in small doses. In large doses it produces a large fall of blood pressure through vaso-dilatation, and cardiac depression, and may also paralyse the vagus inhibitor fibres.

Canadine is closely related to berberine (tetrahydro-berberine) and is much more toxic. It is, however, present in very small quantity in the plant and is of no therapeutic interest.

Hydrastinine and its allies, cotarnine and 6:7-dimethoxy-2-methyl-3:4-dihydro-*iso*-quinoline, have a mild and purely depressant effect on the central nervous system. In very large doses they cause death by paralysis of the respiratory centre.

Hydrastinine causes a moderate rise of blood pressure by: (1) strengthening the heart-beat and increasing the output, in spite of considerable slowing; (2) producing a slight vaso-constriction by direct action on the plain muscle of the arterioles; (3) probably increasing the output of adrenine from the suprarenal body.

Hydrastinine has also a well-marked stimulating action on the uterus. It increases the tonus, the excitability, and the rhythm of the muscle. It is this action which renders it of value in menorrhagia and allied conditions.

Cotarine is on the market under the names of "Stypticine," which is the hydrochloride, and "Styptol" which is the phthalate. 6:7-dimethoxy-2-methyl-3:4-dihydro-*iso*-quinolinium chloride is known as "Lodal." These two allies produce very similar effects to those produced by hydrastinine and have a similar sphere of usefulness in therapeutics. Cotarnine appears to be slightly weaker and causes a transient fall of blood pressure.

Numerous other references will be found in the following selection of papers—

Falk, *Virchows Arch.* (1890), CXIX. 399.
Marfori, *Arch. für exper. Path. und Pharm.* (1890), XXVII. 261.
von Bunge, *Inaug. Diss. Dorpat* (1893).
Ronsse, *Arch. für Pharmacodyn.* (1898), IV. 206; (1899), V. 25.
Williams, *Journ. Amer. Med. Assoc.* (1908), V. 26.
Laidlaw, *Biochem. Journ.* (1910), V. 243.

Preparations.

Hydrastis Rhizoma (B.P., U.S.P.).
Extractum Hydrastis Liquidum (B.P.). 2 per cent. hydrastine.
Dose: 5–15 min. (3–10 dl.).
Tinctura Hydrastis (B.P., U.S.P.).
Dose: ½–1 fl. dr. (2–4 ml.).
Fluidextractum Hydrastis (U.S.P.). 30 min. (2 ml.).
Glyceritum Hydrastis (U.S.P.). 30 min. (2 ml.).
Hydrastina (B.P.C.). ¼–1 gr. (15–60 mg.).
Hydrastininæ Hydrochloridum (B.P.C.). ¼–½ gr. (15–30 mg.).

P. P. L.

COCAINE, EUCAINE AND NOVOCAINE

Coca and its derivatives, although in use for centuries in South America, was not introduced into therapeutics until thirty years ago. The plant is a native of South America, but is now largely cultivated in India, Ceylon and Java. The chief alkaloidal constituent is cocaine, which in the Peruvian and Bolivian leaves is present to about 0·5 per cent., whilst in leaves from Ceylon and Java the proportion of cocaine is lower and other alkaloids such as tropococaine are present in relatively larger quantities.

Cocaine was isolated in 1860, when it was observed that it had the power of producing deadening of sensation in the tongue and mouth. Twenty years later it was shown that the skin became insensitive to pain after hypodermic injections of the alkaloid; but it was not until 1884 that it was first introduced into practical medicine by Koller, who showed its value as a local anæsthetic in ophthalmology; its use then spread to laryngology and later to general surgery.

Cocaine has a powerful action on the central nervous system; the symptoms of poisoning vary considerably in different individuals. In small doses there is excitement, usually pleasurable, though there may be a feeling of anxiety; commonly there is pleasant languor without any marked tendency to sleep. With larger doses the pulse is frequent and there are tremors and muscular spasms, and later convulsions with rapid breathing ending in death. In other cases excitement is absent and the patient suddenly faints and collapses with cyanosis, slow and weak heart action and respiratory failure.

Most of the phenomena are due to stimulation followed by depression of the central nervous system in which the higher centres are first affected. In some cases, the depression appears to occur almost immediately.

The heart is affected chiefly through the nervous system. With moderate doses there is acceleration, which is not due to paralysis of the inhibitory mechanism, for stimulation of the vagus still produces slowing; the acceleration must, therefore, be due either to stimulation of the accelerator mechanism or to a direct action on the muscle itself. In fatal poisoning there is usually slowing before death occurs, probably from the direct action of the drug on the heart muscle. On the vessels cocaine has a powerful effect. There is great vaso-constriction, which is due in the first place to the stimulant effect of the drug on the vasomotor centre, and in the second to its direct action on the muscular walls. The latter is of value in prolonging the local anæsthetic effects of the drug.

When applied locally to mucous membranes or injected subcutaneously cocaine and its substitutes, eucaine, novocaine, etc., paralyse the sensory nerve terminations. The action is direct upon the nerve fibres and is to some extent selective. Nerve fibres conveying sensations of pain and touch are more readily affected than those of heat and cold. When applied to the mouth and nose there is blunting of the sense of taste, especially for bitter substances, and loss of smell. When applied to the unbroken skin there is little or no result unless a solution of the alkaloid itself in a fatty basis is used; this is due to the impermeability of the horny layers of the epidermis, but if this layer be removed by injury or a blister the action of the drug is readily observed. When injected into the region of a nerve trunk cocaine and its allies penetrate into the nerve and abolish the conductivity, thus producing anæsthesia in the region supplied by the nerve.

When injected into the spinal theca cocaine and its allies affect the spinal nerve roots, blocking them and producing widespread anæsthesia sufficient for the performance of amputations and abdominal operations. It is necessary that care be exercised to prevent the extension of the drug too high in the spinal canal in order to avoid danger from paralysis of the diaphragm.

When applied to the eye cocaine produces local anæsthesia, constriction of the conjunctival vessels, and, later, dilatation of the pupil. In its action on the pupil cocaine differs from atropine in many ways. The dilatation is less, the light reflex is not abolished and eserine will produce constriction of the pupil. The dilatation is due to stimulation of the sympathetic terminations in fibres of the dilator pupillæ. After its use the eye should be bandaged, for, owing to the insensitiveness of the cornea, drying with destruction of the superficial cells may readily take place.

In order to avoid the toxic properties of cocaine a large number of substances have been synthesised whose values as local anæsthetics differ considerably; of these eucaine and novocaine are the most valuable. Their solutions can be sterilised by boiling, and are less irritant to the tissues than those of many other derivatives; as anæsthetics they are less powerful than cocaine and differ from it in producing vaso-dilatation. In consequence their anæsthetic action is of shorter duration unless adrenalin be added to produce vaso-constriction and prevent the drug from being washed away from infiltrated area. Since in proportion to its anæsthetic power novocaine is less toxic and less irritant than cocaine, it is generally preferred when used for subcutaneous injection or for infiltration anæsthesia.

Preparations

Coca (U.S.P.). The dried leaves of Erythroxylon Coca containing at least 0·5 per cent. alkaloids.
Dose : 30–120 gr. (2–8 g.).
Fluidextractum Cocæ (U.S.P.). 0·5 per cent. alkaloids.
Average Dose : 30 min. (2 ml.).
Vinum Cocæ (U.S.P.).
Average Dose : 4 fl. dr. (16 ml.).
Extractum Cocæ Liquidum Miscibile (B.P.C.).
Dose : $\frac{1}{2}$–1 fl. dr. (2–4 ml.).
Tinctura Cocæ (B.P.C.).
Dose : $\frac{1}{2}$–1 fl. dr. (2–4 ml.).
Vinum Cocæ (B.P.C.). $\frac{1}{2}$ gr. Cocaine in 1 fl. oz.
Dose : 2–4 fl. dr. (8–16 ml.).
Vinum Cocæ et Quininæ Phosphatis (B.P.C.).
Dose : $\frac{1}{2}$–2 fl. oz. (15–60 ml.).
Extractum Cocæ Liquidum (B.P., 1898.). Composition variable; forms turbidity with water.
Dose : $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

Cocaina (B.P., U.S.P.). An alkaloid derived from coca leaves, insoluble in water, soluble in alcohol oils, fats, etc.
Unguentum Cocainæ (B.P.). 4 per cent.
Oleatum Cocainæ (U.S.P.). 5 per cent.
Nebula Cocainæ Composita (B.P.C.) 0·5 per cent.

Cocainæ Hydrochloridum (B.P., U.S.P.). Very soluble in water and alcohol; aqueous solutions tend to decompose on boiling.
Dose : $\frac{1}{10}$–$\frac{1}{4}$ gr. (6–16 mg.).
Injectio Cocainæ Hypodermica (B.P.). 5 per cent.
Dose : 5–10 min. (3–6 dl.) is half former strength.
Lamellæ Cocainæ (B.P.). $\frac{1}{50}$ gr. (1·3 mg.).
Trochiscus Krameriæ et Cocainæ (B.P.). $\frac{1}{20}$ gr. (3 mg.) in each.
Suppositoria Cocainæ (B.P.C.) $\frac{1}{2}$ gr. (3 cg.) in each.
Pastillus Cocainæ (B.P.C.). $\frac{1}{20}$, $\frac{1}{12}$, $\frac{1}{10}$, $\frac{1}{8}$, or $\frac{1}{6}$ gr. in each.

Benzaminæ Lactas (B.P.). Eucaine Lactate.
Dose : $\frac{1}{8}$–$\frac{1}{2}$ gr. (8–30 mg.). Its action is slower than that of cocaine, it is less toxic and the heart is not affected. Solutions can be sterilised by boiling.

Novocaine.
Dose : $\frac{1}{5}$–1 gr. (12–60 mg.). Very soluble in water. It is less irritant than other cocaine substitutes and less toxic. Solutions withstand boiling. The anæsthesia produced is fugitive owing to its vasodilator action causing its rapid removal. If combined with adrenaline the anæsthesia is lasting and complete. Probably the best local anæsthetic.

Therapeutics.—The internal administration of coca and its derivatives is diminishing steadily. It is much used by the natives of South America, whose endurance is greatly increased by chewing coca leaves; this action is more powerful in the fresh-dried leaves than after importation to Europe. The drug has no power of diminishing metabolism, but it is probable that it acts chiefly by stimulating the motor cortex of the brain and by diminishing the sensations of fatigue and hunger. The preparations of coca are prescribed as "general tonics" and have been recommended as cerebral stimulants; in the latter respect they are inferior to tea and coffee and their alkaloids, which affect more particularly the psychical centres, and are much less dangerous.

The local action on the nerves of the gastric mucosa is of some value in the treatment of vomiting associated with gastritis, pregnancy, etc. Certain much-advertised tonic wines contain considerable quantities of cocaine, and their use has given rise to the cocaine habit. Cocaine has also been used in the treatment of morphinism and is a constituent of certain proprietary remedies for this purpose, but its employment has often been fraught with the disaster of substituting a more serious habit for that which it is sought to cure.

Cocaine Habit.—Many cases appear to arise from attempts to cure the opium or alcohol habit by means of cocaine. The commoner symptoms are loss of appetite, digestive disturbances and emaciation. Sleeplessness, tremors, hallucinations and delirium may occur, mental degeneration sets in and may be well established within six months. Where the drug is taken in snuff there may be epistaxis and ulceration of the mucosa. The treatment of the habit is best carried out in an institution; the drug can be withdrawn completely without fear of untoward symptoms other than those of mental depression.

As a local anæsthetic solutions of 2–4 per cent. are used for the eye, 5–10 or even 20 per cent. for the nose and larynx, and 1–5 per cent. for the urethra. In the nasal passages its action is enhanced and prolonged by the addition of small quantities of adrenalin.

For infiltration anæsthesia solutions of 0·01–0·05 per cent. in 0·8 per cent. saline are employed; adrenalin solution is added in the proportion of 3–5 drops of one per mille solution to every 100 c.c. Novocaine and eucaine are used in a similar manner, but in higher concentration, 0·5 and 0·2 per cent. respectively.

For spinal anæsthesia stovaine is usually preferred.

Intrathecal injection of cocaine and its allies has recently been introduced in the *treatment of strychnine poisoning* with very good results.

They act by blocking the afferent impulses to the cord and thus cut off the stimuli by which the spasms are evoked.

Acute Cocaine Poisoning.—It occasionally happens when cocaine is used as a local anæsthetic in the nose and mouth that the patient suddenly faints and collapses. According to some this is due to an increased susceptibility to the drug, but it is probable that in most cases it is the consequence of unduly rapid absorption, especially from a broken mucous membrane. The treatment is symptomatic; hot-water bottles are advisable and amyl nitrite may be employed if there is much rise of blood pressure; artificial respiration may also be necessary.

Where the drug has been taken by the mouth the stomach should be washed out. Chloroform may be administered when convulsions occur.

Amylocainæ Hydrochloridum (Stovain) is a white crystalline or scaly substance, soluble in water, yielding slightly acid solutions which have an antiseptic action and do not need sterilisation. Alkalies readily decompose the solutions, which should, therefore, be preserved in vessels of Jena glass, and the syringe used for injection should not be sterilised in water to which sodium carbonate has been added. Stovain is a powerful local anæsthetic, but is irritant to the tissues and is likely to cause inflammation; in this respect, therefore, it is less useful for infiltration anæsthesia than is novocain. When used for local anæsthesia $\frac{1}{2}$ per cent. solutions suffice. Stovain is the substance principally used for the production of spinal anæsthesia, sometimes with the addition of adrenalin; some surgeons advocate the addition of strychnine $\frac{1}{100}-\frac{1}{50}$ gr. ($\frac{1}{2}-1$ mg.), when the injection is made in the dorsal region in order to minimise the risk of producing respiratory failure. These high injections have not been found to be devoid of risk.

Dose : $\frac{1}{12}-1$ gr. (5–60 mg.).

HYDROCYANIC ACID, BITTER ALMONDS, VIRGINIAN PRUNE CORTEX, LAUREL LEAVES

The drugs contained in this group may conveniently be considered together, for much of their efficacy is due to their common constituent, hydrocyanic acid. **Hydrocyanic Acid** (prussic acid) when pure is not used in medicine. It is very volatile and its vapour is so poisonous that one or two breaths may be fatal. It is usually met with in dilute solution. The solutions are colourless and possess a characteristic almond-like odour; they should be preserved in small tightly stoppered bottles in a dark cool place in order to avoid decomposition.

In the vegetable kingdom hydrocyanic acid arises from the decomposition of certain glucosides, of which amygdalin and laurocerasin are the chief. The decomposition is brought about by the agency of the enzyme emulsin contained in the superficial layers, whilst the amygdalin is found in the deeper parenchymatous tissues. When the moist kernels or leaves are crushed the enzyme causes hydrolysis of the glucoside with formation of benzaldehyde, glucose and hydrocyanic acid.

Prussic acid is a powerful general protoplasmic poison, but in mammals its chief action is on the central nervous system, which is first stimulated and then paralysed. Largely on account of its rapid absorption its effects are quickly produced, and it is for this reason that prussic acid has earned its popular reputation as a deadly poison, though weight for weight it is less toxic than many alkaloids.

If a large dose be administered to an animal death may occur almost immediately. The animal falls unconscious and after a few gasps and convulsions dies in a few seconds with cardiac and respiratory failure.

In smaller doses there is at first a burning sensation in the mouth followed by numbness. Soon vomiting occurs and is associated with headache and dyspnœa; the heart beats more slowly, there is muscular weakness, and the patient becomes unconscious; convulsions now set in and are followed by paralysis with relaxation of the sphincters, respiration becomes slower, and finally ceases, though the heart may continue beating for a short time.

On the central nervous system the chief action is stimulation followed by paralysis of the medulla oblongata. Thus it causes increased inspiratory movements which, if the dose be not small, are soon diminished, and with fatal doses cease.

The circulatory system is affected in two ways. Stimulation of the medullary centres causes slowing of the heart and generalised vasoconstriction with consequent rise of blood pressure. When this stimulant effect passes off and the blood pressure falls the heart does not regain its normal rate, for its muscle is seriously affected by the action of the poison.

Peripheral sensory nerves are paralysed by the acid; this is evidenced by the numbness produced in the tongue. It is probable that the utility of prussic acid in the treatment of vomiting in gastritis depends upon its analgesic action on the nerves of the gastric mucosa. It is also for the analgesic action of its prussic acid that cherry-laurel water is used as a constituent of eye lotions.

Hydrocyanic acid appears to act as a general protoplasmic poison by depriving cells of their power of utilising oxygen. It is known that the acid and its salts inhibit the action of many

enzymes *in vitro*, and it is probable that the oxidative processes of the body are the result of enzyme activity. This hypothesis will explain the facts that in spite of the convulsions the venous blood remains bright red and the oxygen absorption and carbonic acid output fall almost to zero.

Prussic acid is rapidly destroyed in non-fatal cases; portions are converted to sulphocyanides and excreted in the urine, whilst others are dealt with in unknown ways.

Prussic acid is incompatible with salts of iron, silver, mercury.

Therapeutics.—Prussic acid is not very extensively used nowadays. It is sometimes applied externally in pruritus to allay irritation, but should be used with caution, for owing to its rapid absorption from a broken surface toxic symptoms may readily arise. Internally it is used in the treatment of vomiting, especially of acute gastritis and pregnancy, where it appears to be efficacious. Formerly it had a considerable vogue as a constituent of cough mixtures, but it is doubtful whether it is of great value except for the reflex cough of gastric irritation. Most of the formulæ in which it was included contained also morphine or opium in quantities sufficient to produce the effects attributed to the acid.

Poisoning.—In most cases of poisoning by prussic acid death occurs before medical aid can arrive. The treatment follows the general principle of washing out the stomach and applying warmth. Ammonia may be given or inhaled as a respiratory stimulant and artificial respiration applied, although it is not probable that it will be of much value owing to the simultaneous poisoning of the heart. The intravenous injection of sodium sulphide and thiosulphate has been suggested with the object of forming innocuous substances. Since prussic acid rapidly disappears from the tissues the object of the treatment is to tide the body over the period during which its oxidative processes are in abeyance.

Preparations

Acidum Hydrocyanicum Dilutum (B.P., U.S.P.). A 2 per cent. solution. It is unstable and tends to deteriorate.
Dose: 2–5 min. (12–30 cl.).

Mistura Acidi Hydrocyanici Composita (B.P.C.). This preparation is used as a cough mixture, especially in phthisis. It contains $2\frac{1}{2}$ minims of the dilute acid and $7\frac{1}{2}$ minims of Liq. Morphinæ Hydrochlor. in 4 fluid drachms.
Dose: 2–4 fl. dr. (8–15 ml.).

Dilute Hydrocyanic acid is also contained in Tinct. Chloroformi et Morphinæ Co. to the extent of 1 in 20. Numerous other preparations contain varying quantities of the acid, *e. g.* those of bitter almonds, Virginian prune, laurel—see below.

Bitter Almonds are the seeds of Prunus Amygdalus, var. Amara; they may readily be distinguished from sweet almonds by their taste and their characteristic smell when ground under warm water.

On expression they yield about 40–50 per cent. of fixed oil, which is the commercial almond oil; they also contain amygdalin and emulsin. The residue after expression is mixed with warm water, when the emulsin gradually hydrolyses the amygdalin to glucose, benzaldehyde and hydrocyanic acid; the mixture is then distilled in a current of steam, when the benzaldehyde and hydrocyanic acid distil over. It is probable that they are for the most part combined loosely to form benzaldehydecyanhydrin. They separate out at the bottom of the water as essential oil of almonds, which may contain about 5 per cent. of hydrocyanic acid. The essential oil may be deprived of its contained prussic acid and is then used largely as a flavouring agent.

Chemically there is no relation between Oleum Amygdalæ and Oleum Amgydalæ Amaræ, the essential oil, and since the latter is toxic and contains prussic acid it is better to order it when required under the name of Essential Oil of Bitter Almonds and to specify whether the prussic-acid-free oil is required or not. The latter consists of benzaldehyde.

Therapeutics.—Derivatives of bitter almonds are important for their three main constituents, the fixed oil, the essential oil and the hydrocyanic acid. The fixed oil is much used for fine toilet preparations and internally as a pleasant nutritive fat, also, when sterilised, as a lubricant for catheters, etc. The essential oil with its hydrocyanic acid is used in the same way as the acid (see above); the oil from which the acid has been removed is used as a flavouring agent for medicinal and culinary purposes.

Preparations

Mistura Amygdalæ Amaræ (B.P.C.). Used as a basis for lotions to allay skin irritation.

Mistura Amygdalæ Amaræ Composita (B.P.C.). Used as a cough mixture, the content of hydrocyanic acid is variable.
Dose: $\frac{1}{2}$–1 fl. oz. (15–30 ml.). 1 part of compound powder in 8.

Pulvis Amygdalæ Amaræ Compositus (B.P.C.). Used in making the above mixture.

Oleum Amygdalæ (B.P., U.S.P.). May be obtained from either sweet or bitter almonds.
Dose: 1–4 fl. dr. (4–16 ml.).

Ceratum Galeni (B.P.C.). Contains 50 per cent. almond oil. Used for toilet purposes.

Emulsio Olei Amygdalæ (B.P.C.). A 12·5 per cent. emulsion, used as a cough mixture.
Dose : 2–8 fl. dr. (8–30 ml.).

Lotio Crinalis (B.P.C.).

Oleum Amygdalæ Amaræ or Oleum Amygdalæ Essentiale (U.S.P.). The essential oil should contain 2–4 per cent. of prussic acid.
Dose : $\frac{1}{4}$–1 min. (1–6 cl.).

Aqua Amygdalæ Amaræ (U.S.P.). 1 in 1000.
Dose : $\frac{1}{2}$–2 fl. dr. (2–8 ml.). For flavouring.

Spiritus Amygdalæ Amaræ (U.S.P.). Essence of bitter almond is used chiefly for flavouring.
Average dose : 8 min. (5 dl.).

Syrupus Amygdalæ (U.S.P.).
Average dose : 1 fl. dr. (4 ml.).

Oleum Amygdalæ Amaræ sine Acido Prussico.

Essentia Amygdalæ Composita (B.P.C.). Compound essence of almond is prepared from the prussic-acid-free oil and contains vanilla and benzoin. It is used for flavouring.

Virginian Prune Bark.—The bark is derived from young stems of Prunus serotina, and should be collected in autumn.

The chief constituents are a glucoside allied to amygdalin, and an enzyme similar to, if not identical with, emulsin; it also contains a bitter glucoside and some tannin. When bruised in the presence of water the emulsin hydrolyses the glucoside, with the production of benzaldehyde and hydrocyanic acid and the odour of bitter almonds.

Preparations of Virginian prune act chiefly in virtue of the hydrocyanic acid which they contain.

Therapeutics. — Preparations of Virginian prune owe their efficacy to the hydrocyanic acid which they contain (for mode of action see under *Hydrocyanic Acid*). They are also used as flavouring agents in cough mixtures.

Preparations

Fluidextractum Pruni Virginianæ (U.S.P.).
Average dose : 30 min. (2 ml.).

Infusum Pruni Virginianæ (U.S.P.). This preparation is weaker than the tincture and is used as an addition to cough mixtures.
Dose : 1–2 oz. (30–60 ml.).

Syrupus Pruni Virginianæ (B.P., U.S.P.). A sedative for use in cough mixtures in phthisis and bronchitis.
Dose : $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

Tinctura Pruni Virginianæ (B.P.).
Dose : $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

None of these preparations is standardised as regards its content of hydrocyanic acid.

Laurel Leaves.—The leaves of the Cherry-laurel (Prunus Laurocerasus) are official. Their most important constituent is the glucoside laurocerasin, which, though not identical with amygdalin, closely resembles it. The glucoside is situated in the superficial layers, whilst the enzyme emulsin resides in the vascular bundles; hence the intact leaf is odourless, but when bruised so as to permit the emulsin to come into contact with the glucoside hydrolysis ensues with the production of benzaldehyde, glucose and hydrocyanic acid, and the characteristic bitter almond odour develops. The action of cherry-laurel water depends on the hydrocyanic acid which it contains (see under *Hydrocyanic Acid* above).

Therapeutics.—Cherry-laurel water is used externally as a constituent of eye lotions when diluted about fifteen times.

Internally it is used as a flavouring agent (see above under *Hydrocyanic Acid* and *Bitter Almonds*).

Preparation

Aqua Laurocerasi (B.P.). Prepared by distilling a mixture of crushed leaves and water and adding dilute hydrocyanic acid or diluting the distillate with water until it attains the requisite strength. This preparation is standardised to contain 0·1 per cent. of pure hydrocyanic acid, and must be preserved in well-stoppered bottles.
Dose : $\frac{1}{2}$–2 fl. dr. (2–8 ml.). P. H.

DIURETICS

Diuretics are substances which produce an increase in the amount of urine excreted.

Before discussing the various ways in which diuretics act, it may be well to consider briefly the physiology of diuresis. It may be stated that we still have very little more than theory to rely on; the state of our knowledge of the mechanism of diuresis is at the present day but slightly more satisfactory than it was in the days of Bowman, Heidenhain and Ludwig. Does the kidney excrete urine by means of vital processes, exercising a selective action and picking out certain substances from the blood and eliminating them in the urine, whilst it leaves other substances behind in the blood? On the other hand, is the excretion of the urine the result of physical processes? To these questions we can give no definite answers, and between these two bald hypotheses there are many shades of opinion.

Without going into details and without dis-

cussing the arguments for and against the rival theories, it will suffice for the purposes of this article to bear in mind that it is possible for the glomeruli to excrete a fluid more or less resembling urine by simple osmosis, but that osmosis alone cannot account for the whole process of diuresis. Further, the renal tubules *may* excrete, and they *may* also reabsorb water from the glomerular excretion as it passes down from the glomeruli towards the ureter; again, the glomeruli *may* act as propulsors, as suggested by Brodie. Still further, one must bear in mind the fact that active work is done by the kidneys, during copious diuresis at all events. It does not follow, of course, that all these methods of excretion are made use of at the same time, if at all. It is perhaps possible that the small amounts of urine excreted during the resting stages of the daily output may be excreted by osmosis alone, with a certain amount of the excreted water being reabsorbed as it passes through the renal tubules; and that the larger amounts of urine passed some time after a meal or after the ingestion of water or of diuretic drugs may depend in part at any rate on some active stimulation of the renal epithelium, though exactly how this may be accomplished we do not know. With these prepositions before us it is easy to understand the ways in which certain diuretics may act.

The normal mechanism of diuresis may depend on—

1. The state of the glomeruli.
2. The state of the renal tubules.
3. The composition of the blood flowing to the kidneys.
4. The general arterial blood pressure.
5. The rapidity of the blood flow through the kidneys.
6. The arterial pressure within the kidneys.
7. The innervation of the kidneys.

Thus it is conceivable that a diuretic may act by affecting any one or more of these factors.

Diuretics may be classed as: (*a*) Direct and (*b*) Indirect. To the first class belong such substances as, reaching the kidneys in the blood, produce an increased secretion of urine, either by direct stimulation of the renal epithelium, as is possibly the case with substances not normally present in the blood, or by the production of an increased osmotic pressure, as appears likely to be the case when one of the normal constituents of the blood is present in excess of its normal amount. To the second class belong substances which produce an increased flow of urine by raising the blood pressure, increasing the rapidity of the blood flow through the kidneys or by causing nervous stimuli to reach the kidneys. It is, of course, possible and even likely that many diuretic substances act as such in more ways than one. Caffeine, for example, almost certainly stimulates the renal epithelium, and there is no doubt that it causes an increased rapidity of blood flow through the kidneys.

Diuretics may be tabulated as follows—

Direct	Essential Oils. Purin Derivatives. Salts—see also chapter on *Salt-Action*. Water.
Indirect	Digitalis group. Purin Derivatives.

Besides these the application of cold to the skin, emotional stimuli, etc., act as diuretics, the former probably by diminishing or suspending the elimination of fluid by the sweat glands, and the latter either by acting reflexly and causing direct nervous stimuli to reach the kidneys or it may be by checking skin action in the same way as cold. Furthermore, it is possible that endogenous bodies or internal secretions may play no small part in the mechanism of diuresis. Also, urea is known to possess strong diuretic powers: this substance probably has a wide influence in maintaining the normal process of diuresis.

From the foregoing remarks it would appear that innumerable substances should act as diuretics, as doubtless they would; but it must not be forgotten that certain substances only produce an increase in diuresis under certain conditions: *e. g.* digitalis and its congeners, which are efficient and most useful diuretics in such conditions as mitral disease, where the diminished diuresis is due to failing cardiac action. Under normal conditions, on the contrary, these drugs cannot be classed as diuretics, for with the heart performing its functions in an efficient manner the exhibition of digitalis will not produce the slightest increase in the amount of urine voided.

Other bodies, again, that provoke an increased flow of urine may produce this effect by reason of their irritative properties; such bodies, for instance, as cantharides and turpentine, if introduced into the circulation, will provoke, temporarily at any rate, an increased flow of urine; but from this very property of irritation they are useless as routine diuretics, for their continued use would sooner or later induce a condition of nephritis.

It must not be supposed from these remarks that all substances which produce an increase in diuresis from their stimulating effect on the renal epithelium must for that reason be unworthy of consideration as useful therapeutic agents: many substances which probably act in this way are so slightly irritant that they may be given with impunity for a short time, though if given over a long period their action might be

not altogether free from harm. One might suppose that if such substances are so slightly irritant their effect as diuretics would be so slight as to be negligible; but the kidney seems to have a peculiar property of isolating and collecting within itself any foreign bodies, toxic or otherwise, that may be circulating in the blood, so that the action of such substances becomes concentrated, as it were, on the kidneys. In this connection one may call to mind the extraordinary frequency with which the kidneys are affected in so many of the fevers and general intoxications, whilst other organs escape as a rule without damage. There are many diuretic substances which probably act by a slight irritant and stimulating action on the renal epithelium, such as copaiba, cubebs, buchu, juniper and ononis.

In therapeutics, then, from the point of view of the kidney at any rate, those diuretics should be best which act in a more or less indirect manner, rather than those which directly stimulate the renal epithelium. There is, for instance, some evidence that over-indulgence in the use of tea and coffee as beverages carried on over a number of years tends to produce a certain degree of nephritis, caused presumably by the continued ingestion of caffeine, though a single cup of tea may be said with truth to be harmless.

Purgatives as Diuretics.—There is one class of drugs which for diuretic purposes does not appear to have met with the attention it deserves: I refer to certain purgatives. In the majority of cases in which it is desirable to administer a diuretic, a certain looseness of the bowels will do no harm; rather will it be beneficial. Moreover, those purgatives which owe their action to the pouring out of fluid into the intestine and which produce watery stools, act for the most part as most efficient diuretics. What probably happens is that fluid is poured out from the tissues into the intestine owing to the irritant action of the purgative, and that before this can be voided by the rectum with the fæces a part of this extravasated fluid is reabsorbed into the blood stream, and this reabsorbed fluid on reaching the kidneys excites them to action, with an abundant excretion of urine. There is a certain amount of experimental evidence which lends support to this view, but until the matter has been further investigated it must be regarded as being *sub judice*. The addition of a little opium to the purgative will delay the excretion by the rectum, and allow more time for the reabsorption of fluid from the intestine, thus increasing the diuretic action if this is desirable.

Diuretic Salts.—A large number of inorganic salts are diuretic: these owe their action chiefly to osmosis, as described in the chapter on *Salt-Action* (*q. v.*). It may be pointed out here that any salt finding its way into the circulation will act as a diuretic, even those that are normally present in the blood if they are in excess of their normal amount.

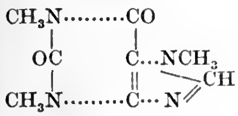
Alcohol.—Alcohol acts as a diuretic, but not to the extent that might be supposed. When alcohol is taken in the form of beverages, a greater or smaller quantity of water is taken with it; sometimes, indeed, enormous quantities of fluid are drunk in this form, far more than can possibly be required to quench thirst; so that a large proportion of the resulting diuresis must be ascribed to the volume of water imbibed. Alcohol has, however, a slight diuretic action *per se*. This is due partly to increase in cardiac action and increase in blood pressure, and partly in all probability to a direct action on the renal epithelium, as a small percentage of the alcohol imbibed is excreted in the urine.

There are many substances, for the most part extracts and infusions of various plants, which have been used empirically as diuretics for a long time, in many cases by the laity as household remedies, and which have not received due recognition from the medical profession. Amongst these may be mentioned juniper, equisetum (mare's tail), ononis (rest harrow), petroselinum (parsley), kava (a vegetable infusion used by the South Sea islanders) and many others. Of these equisetum and petroselinum are but feeble in action: ononis is distinctly more potent (I have seen 20 c.c. of a watery extract of this substance given by mouth to a dog produce an excretion of as much as 80 c.c. of urine in 80 minutes, the previous rate of excretion being at the rate of 12 c.c. in 80 minutes); moreover, this drug is not so irritant as juniper, which in large doses may produce bloody urine. Apart from its diuretic action kava appears to have a stimulating action on the central nervous system, followed, when taken in large quantities, by a paralysing action on some part of the nervous system.

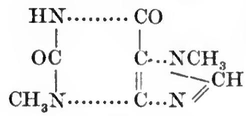
Water.—Water is diuretic both by reason of its bulk, in that it dilutes the blood after absorption and provokes an increase in diuresis by osmosis, and probably also owing to its taking up some substance during the process of absorption, which excites the kidneys to increased activity. It is a remarkable fact that water given by the mouth and absorbed from the gastro-intestinal tract provokes a far more copious diuresis than does the same quantity injected subcutaneously or intravenously. In conjunction with this, one recalls to mind the fact that none of the usual diuretic drugs produces its effect in any considerable degree when injected, though when given by the mouth the diuretic effect may be considerable.

Caffeine.—Both caffeine and theobromine, as also is theophylline, are purin derivatives; theobromine with its isomer, theophylline,[1] being dimethylxanthin, having two CH_3 radicles, and caffeine with three CH_3 radicles being trimethylxanthin. Their formulæ are as follows—

Caffeine.



Theobromine.



Caffeine (syn. theine, guaranine) is an alkaloid obtained from tea, coffee, kola and other plants, whilst theobromine is an alkaloidal constituent of cocoa.

Caffeine is easily absorbed and has no important action on the gastro-intestinal tract. It is excreted largely in the urine in the form of xanthin bodies.

Caffeine as a Diuretic.—Caffeine exerts a powerful action as a diuretic, and its action as such is rather complex. Certain established facts must be borne in mind—

1. Caffeine quickens the heart and renders its beat rather more forcible.
2. It constricts the blood-vessels.
3. The renal blood-vessels are said to dilate after an initial constriction whilst the other vessels still remain constricted, though finally all the vessels dilate.
4. During the period of increased diuresis the kidneys take up more oxygen than normally.
5. A large part of the caffeine is excreted by the kidneys in the form of xanthin bodies.

Now the first two factors obviously induce an increased blood pressure, and this, taken in conjunction with the third factor, produces an increased quantity of blood flowing through the kidneys—a favourable condition for the production of increased diuresis by simple osmosis. The fourth factor, however, does not fall into line with the theory that caffeine acts as a diuretic simply by producing conditions favourable to osmosis. The increased absorption of oxygen and the fact that so large a proportion of the caffeine is excreted in the urine would lead us to the conclusion that caffeine excites the renal epithelium to do active work; and this under the most favourable conditions for the excretion of urine by osmosis. In all probability, then, caffeine acts as a diuretic both by causing more blood to flow through the kidney in a given time, and so increasing osmotic action, and also by directly stimulating the renal epithelium to activity.

Caffeine on the Central Nervous System.—Besides its action as a diuretic caffeine has other important actions. Caffeine stimulates the central nervous system: at first the action is on the higher centres; thought becomes easier, the association of ideas is more rapid, the sense of fatigue vanishes and a condition of extreme wakefulness ensues. It is a matter of common experience that tea- or coffee-drinking in the late evening is a fruitful cause of insomnia; also that during a bout of hard brainwork an occasional cup of tea greatly facilitates the working of one's thoughts. If small doses only are taken no further action on the central nervous system is apparent; but after large doses the initial stimulation of the higher centres is followed by stimulation of the motor areas, with general excitement and restlessness, which quite overshadows the action on the higher centres, so that the prevailing feeling of excitement effectually prevents any further attempts at the exact co-ordination of ideas. Following on this stimulation of the motor areas stimulant effects are observed (with large doses only) to proceed downwards to the medulla and spinal cord, increased excitability, vaso-constriction, increased depth of respiration, exaggerated reflexes, trembling, spasmodic movements, and, finally, convulsions ensuing.

Caffeine on Muscle.—To striated muscle caffeine acts as a direct stimulant: after caffeine the muscles are able to perform more work, other things being equal, than without caffeine, so that this fact, taken in conjunction with its action on the higher centres in banishing fatigue, affords at any rate a partial explanation of the results of the oft-quoted experiments on soldiers on the march: those companies marching on cocoa coming out of the ordeal far better than those marching on alcohol or meat extracts. But the possible effects of the sugar and fat contained in cocoa must be borne in mind in drawing any conclusions from these experiments.

Caffeine on Blood-vessels.—The chief action of caffeine on plain muscle is a marked one of dilating blood-vessels. In the intact animal this dilatation of the blood-vessels is preceded by a constriction of central origin: this initial constriction after a time passes off and gives place to dilatation, which is due to a peripheral action on the musculature of the blood-vessels. All the vessels dilate to caffeine whether they are supplied with vaso-dilator nerves or not.

Caffeine on Cardiac Muscle.—On cardiac muscle, too, caffeine has an action. It produces an acceleration in the rate of heart-beat, the diastolic pause being curtailed. There is no great change in the amplitude of the beat, any difference that is observable being in the direction of increase in force and amplitude. The quickening can be demonstrated by perfusing

[1] Theocin sodium acetate is chemically Theophylline-Sodio Sodium Acetate.—Ed.

an isolated heart, so that the action is peripheral and not due to the caffeine effect on the central nervous system. It also occurs after the administration of atropine and apocodeine, so that the quickening is not due to vagus or sympathetic action. We must, therefore, come to the conclusion that the increased rate of heart-beat is due to a direct action on the cardiac muscle.

Other Purin Derivatives.—All the purin bodies have, roughly speaking, the same action, different members of the series varying only in degree as regards their actions. Thus the action of theobromine on muscle is more marked than its action on the central nervous system, as compared with caffeine. As a general rule it may be stated that members of the purin group vary in their diuretic power directly as their power of acting on blood-vessels varies : and this perhaps may be used as an argument in favour of the theory that their diuretic action is due solely to their power of enabling more blood to flow through the kidneys in a given time.

Caffeina (B.P., U.S.P.). $C_8H_{10}N_4O_2.H_2O$. White silky crystals with a bitter taste, soluble in water 1 in 80.
Dose : 1–5 gr. (6–30 cg.).

Caffeinæ Citras (B.P.). Caffeina Citrata (U.S.P.). $C_8H_{10}N_4O_2.C_3H_4(OH)(COOH)_3$). White powder, soluble in water 1 in 32. Incompatible with Potassium Iodide and Spirit of Nitrous Ether, also with Sodium Salicylate.
Dose : 2–10 gr. (12–60 cg.).

Caffeinæ Citras Effervescens (B.P., U.S.P.). Contains 4 per cent. of the citrate.
Dose : 60–120 gr. (4–8 g.).

Theobrominæ et Sodii Salicylas (B.P.). "Diuretin," a white amorphous powder, soluble in water 1 in 1.
Dose : 10–20 gr. (6–12 dg.).

Buchu.—The leaves of Barosma betulina (Rutaceæ), which when dried contain about 1–2 per cent. of a volatile oil.

Buchu as a Diuretic.—Buchu owes its activity as a diuretic entirely to the volatile oil which it contains; and this, as other volatile oils, is partly excreted by the kidneys in combination with glycuronic acid. The slightly irritant action produces a dilatation of the renal vessels, and in all probability it also excites the renal epithelium to activity, the result at all events being an increase in the amount of urine excreted.

Buchu as an Antiseptic.—Like the other volatile oils, too, it has a slight antiseptic action, and therefore is particularly suitable when there are micro-organisms flourishing in the bladder and other urinary passages. Volatile oils when undiluted are efficient germicides, though in the state of dilution in which they reach the urinary passages this antiseptic action can be but slight.

Buchu has also slight carminative and expectorant properties, these also being due to the volatile oil.

Buchu Folia (B.P.). Buchu (U.S.P.).
Infusum Buchu (B.P.).
Dose : 1–2 fl. oz. (30–60 ml.).
Tinctura Buchu (B.P.).
Dose : ½–1 fl. dr. (2–4 ml.)
Fluidextractum Buchu (U.S.P.).
Dose : 30–60 min. (2–4 ml.).

Scoparium.—Scoparii Cacumina are obtained from the leaves and branches of broom (Cytisus Scoparius).

The broom-tops contain an alkaloid, sparteine, a volatile oil, tannin and scoparin, a yellow crystalline body.

Little is known of the pharmacological action of scoparium. It is freely used as a diuretic, though to be sure the infusion is more often than not used as a vehicle for other diuretics when given in mixture form. It is probable that the diuretic action of scoparium is not great. Sparteine has a slight diuretic action, though not comparable to that of caffeine, its chief effect being a paralysing one on motor nerves. The volatile oil, like others, has some diuretic action. Scoparine has been stated to be the diuretic element in scoparium, though it appears likely that its action as a diuretic is extremely slight, if it has any diuretic action at all.

The constituent principles of scoparium have not gained a good reputation as therapeutic agents, and the drug is more frequently prescribed in the form of the infusion when the diuretic effect is desired at all events.

Scoparii Cacumina (B.P.). Scoparius (U.S.P.)
Infusum Scoparii (B.P.).
Dose : 1–2 fl. oz. (30–60 ml.).

Succus Scoparii (B.P.).
Dose : 1–2 fl. dr. (4–8 ml.).

Scoparinum (B.P.C.). $C_{19}H_{16}O_8(OH)(OCH_3)$.
Dose : 5–8 gr. (3–5 dg.).

Saparteinæ Sulphas (U.S.P.).
$C_{15}H_{26}N_2H_2SO_4.5H_2O$). Colourless crystals, soluble in water 3 in 2.
Dose : ¼–1 gr. (16–60 mg.).

Uva Ursi.—Uvæ Ursi Folia (Bearberry leaves) are obtained from Arctostaphylos Uva-ursi (Ericaceæ), and contain a large proportion of tannin, some gallic acid, two crystalline glucosides, arbutin and methyl-arbutin and other bodies.

The arbutin is for the most part excreted unchanged by the kidneys; part, however, is split up, forming hydroquinone, which gives a

greenish colour to the urine. The diuretic action of uva ursi is probably due to the arbutin which it contains.

Uvæ Ursi Folia (B.P.). Uva Ursi (U.S.P.).
Infusum Uvæ Ursi (B.P.).
Dose : ½–1 fl. oz. (15–30 ml.).
Infusum Uvæ Ursi Concentratum (B.P.C.).
Dose : ½–1 fl. dr. (2–4 ml.).
Fluidextractum Uvæ Ursi (U.S.P.).
Dose : 1–4 fl. dr. (4–16 ml.).

D. C.

URINARY ANTISEPTICS

1. *General Considerations.*—A urinary antiseptic is a drug given by the mouth with a view to its exerting a disinfectant action in the urine and the urinary tract. In considering the urinary antiseptics proper it is convenient to describe also certain drugs which alter the reaction of the urine and are used as adjuvants to them.

So little is known as to the chemical form in which many of these drugs are excreted, that in view of the possibilities in so complex a chemical solution as urine, it must be borne in mind that the value of a substance as an antiseptic outside the body is not necessarily a criterion of its value when secreted in urine. This value may be enhanced or diminished. None the less, in considering the credentials of any such drug it is always worth inquiring—in what strength of solution will the drug exist in the urine when given in ordinary doses? From what we know of its power as a disinfectant is it likely to be reasonably effective in that strength of solution? For example, salol (phenyl-salicylate) has been used as a urinary antiseptic. In ordinary doses the phenol element cannot exist in the urine in a greater strength than about 1 in 1000. Now phenol added to urine in this strength has no antiseptic action. It is, therefore, unlikely that the drug possesses any advantage over other salicylates.

Looked at from this point of view it will be found that few substances can be given which are excreted in the urine in sufficient amount to be very effective. It is necessary that the substance excreted must be a very powerful antiseptic, or the dose must be very large. The only known substance which possesses strong antiseptic power in a solution of 1 in 10,000, and which can be made to appear in the urine, is formaldehyde. Consequently it is not surprising to find that the group of drugs which cause it to be excreted are the most powerful of the urinary antiseptics, though their action is unfortunately limited to acid urine.

And this brings out another point. The reaction of the urine and its degree of acidity or alkalinity are all-important; most organisms which grow in urine are inhibited by acidity, but some are encouraged by it, while the action of most drugs is affected by it. So that one cannot say of a urinary antiseptic that it is a good-all-round drug. The reaction of the urine and the type of organism must be considered.

Again, it must be borne in mind that these drugs can only be expected to prevent the growth of bacteria in the urine itself (most bacteria grow readily in urine) and on the surface of the mucous membrane of the urinary tract. They will not do much good where the deeper tissues are affected. And, although clinical evidence must always have the last word here, as elsewhere, much of that adduced in support of new drugs is really worthless. The drugs are tried in a limited number of different cases, they are not compared in any way with older drugs, other measures are used simultaneously, and an improvement in the patient's condition is attributed without any evidence to the drug. Recognising this, a fair amount of purely experimental work has been done lately with regard to many of these drugs. Some of it has taken the form of simply estimating their value as antiseptics; a far more profitable type of work is that in which the drugs have been given by the mouth and the antiseptic power of the resulting urine examined—either by mixing it with cultures, or, better still, by growing organisms in the urine direct and noting the inhibitory effect of the drug present.

The adjuvant drugs most commonly used are the citrates with sufficient doses (1 dr. or more), of which the urine is rendered alkaline, and the acid phosphate of sodium (NaH_2PO_4) which is undoubtedly the most efficient drug for increasing the urinary acidity.

Urine, which is constantly alkaline, is probably never secreted by the kidney on a normal diet and apart from drugs. A persistently alkaline urine is always due (with the above exception) to ammoniacal fermentation in the bladder. No drug will render such urine acid except by stopping the fermentation.

Consequently acid sodium phosphate only assists the antiseptics in these cases by increasing the acidity of the urine coming down from the kidney. This drug given in the largest doses ordinarily tolerated, about doubles the acidity of the urine. No other drug increases it by more than a half, and there are only very few other drugs (*e. g.* salicylates and benzoates) which increase acidity at all appreciably.

Note.—In prescribing acid sodium phosphate the alkaline phosphate (Na_2HPO_4) of the pharmacopœia is liable to be substituted unless

some further note is made as to what is wanted —perhaps it is best to write sodium di-hydrogen phosphate or give the formula (NaH_2PO_4)—the solution of the salt is strongly acid to litmus.

List of the principal Urinary Antiseptic Drugs, with the form or preparation in which they are commonly given; and the dose.

Division I.—Ammonia-formaldehyde Compounds.

Drug.	*Form or Preparation.*	*Dose.*
Hexamethylene-tetramine = "Urotropin"	Hexamina (B.P.) As such in solution.	5–15 gr. (3–10 dg.).
Hexamethylene-tetramine-anhydromethylene-citrate = "Helmitol"	As effervescent tablets.	5–15 gr. (3–10 dg.).

Division II.—Coal-tar Products.

Drug.	*Form or preparation.*	*Dose.*
Benzoic Acid.	Ammonium Benzoate.	5–15 gr. (3–10 dg.).
Salicylic Acid.	Sodium salicylate.	15–25 gr. (10–15 dg.).
Salol.		5–15 gr. (3–10 dg.).

Division III.

Drug.	*Form or preparation.*	*Dose.*
Boric Acid.	As such in solution.	15–25 gr. (10–15 dg.).

Division IV.—Essential Oils.

Drug.	*Form or preparation.*	*Dose.*
Sandal Wood Oil.	As such in cachets *or* in emulsion.	20–30 min. (12–18 dl.).
Santalol salicylate = "Santyl"	As such in milk.	30–40 min. (18–25 dl.).
Copaiba.	As Ol. Copaibæ in emulsion.	10–20 min. (6–12 dl.).
Cubebs.	As Ol. Cubebæ in emulsion.	10–20 min. (6–12 dl.).

Division V.—Vegetable Infusions and their Derivatives.

Drug.	*Form or preparation.*	*Dose.*
Uva Ursi.	Infusum Uvæ Ursi.	½–1 fl. oz. (15–30 ml.).
Arbutin.	As such in solution in water.	15–30 gr. (1–2 g.).
Buchu.	Infusum Buchu	½–1 fl. oz. (15–30 ml.).

Division I.—Hexamethylenetetramine and its Derivatives

Hexamethylenetetramine is a readily soluble white crystalline powder, formed by the combination of ammonia and formaldehyde. It is stable in alkaline or neutral solution, and is dissociated by acids with the liberation of formaldehyde—this dissociation depending upon temperature and strength of solution but taking place to a considerable extent in acid urine at body temperature. It was discovered by Butlerow in 1860, but was not used as a drug until 1894, when Nicolaies introduced it as a solvent of uric acid. This action is now discredited, but its value as a urinary antiseptic has come to be beyond dispute. It was sold under the name of urotropin, which it is still familiarly called. Although there has been some dispute about the action of this drug, there is little doubt that the following facts are true. The substance itself is not an antiseptic at all. It acts solely by the dissociation of a certain proportion of it yielding formaldehyde. This only takes place in an acid urine and the proportion of formaldehyde varies with the acidity. If the acidity is high the urine will not support the life of any organism, and in such urine this substance is far the most powerful of all the urinary antiseptics. In alkaline urine it is inert. Hexamethylenetetramine has been sold under a large number of different names, *e. g.* Formamine, Cystogen, Urisol, etc., but in addition certain derivatives of it have been produced which are claimed by their makers as improvements. The most notable of them is helmitol, which is hexamethylenetetramine anhydromethylene citrate. This substance possesses the property of readily yielding formaldehyde under the influence of both acids and alkalies, and in consequence it was hoped that it would act well in alkaline urine. When given by the mouth the hexamethylenetetramine element acts as such. As to the fate of the other element there is some doubt; there seems to be some evidence that it is dissociated in the blood yielding formaldehyde, but so far there are no pharmacological facts to support the view that helmitol yields formaldehyde in alkaline urine, or that it possesses any advantages over hexamethylenetetramine as a urinary antiseptic. Indeed, even if formaldehyde were secreted into an alkaline urine, it would not exist for long in the presence of ammonia at body temperature.

Other derivatives of hexamethylenetetramine which have been introduced are citramine, which is a mixture of urotropin and helmitol; hetraline, which is hexamethylenetetramine dioxybenzene, and, more recently, cystopurin, which is a combination or mixture of hexamethylenetetramine with sodium acetate. The amount of this latter in a dose is so small that it is probably negligible. If this were not the case, by reducing the acidity of the urine its action would be positively harmful. Probably, therefore, the action of this combination is inferior to that of simple hexamethylenetetramine.

Hexamethylenetetramine in Cerebro-spinal Fluid and Bile.—The fact that this substance is

excreted in other secretions beside urine has often been demonstrated. It has been found in appreciable quantities in cerebro-spinal fluid, bile, and saliva, and it is likely that so readily soluble a substance permeates the tissue fluids generally. This naturally suggested its use as a disinfectant of these fluids, and it has been used considerably in meningitis, as a prophylactic against meningeal infection before operation in compound fractures of the skull, etc., and to a less extent in cholecystitis; it has also been given in pericarditis, synovitis, etc. There is a certain amount of clinical evidence as to its value in cerebro-spinal fluid and bile. From what has been said above as to the action of this substance, it will be apparent that, since all these fluids are alkaline, one would not expect to get any appreciable antiseptic action. None the less, the faintly alkaline and ammonia-free cerebro-spinal fluid is very different from alkaline urine, and if any formaldehyde were present there it would continue to exist and exert its action. So that these drugs are certainly worth further trial in this connection, and owing to its properties "Helmitol" would appear likely to be the most efficient.

Division II.—The Coal Tar Derivatives

Benzoic Acid, Salicylic Acid, Salol

Benzoic acid, given usually in the form of the ammonium salt, has long been recognised as a useful urinary antiseptic. It gives rise to the formation of hippuric acid in the urine, and it has the effect of decidedly increasing the urinary acidity, being in this respect only surpassed by acid sodium phosphate. It has a decided antiseptic action in acid urine, but its action in alkaline urine is very much more feeble. It inhibits the B. coli to some extent, but is less effective, relatively, against the staphylococcus.

Salicylic acid is less frequently employed as a urinary antiseptic. It is excreted as a mixture of salicylic and salicyluric acid. Both these substances are antiseptics of much the same power, and the general action of the drug is very similar and slightly inferior to benzoic acid. It is said to increase the urinary acidity, but only does so to a very small extent. It also is almost inert in alkaline urine.

Salol (phenyl-salicylate), as a urinary antiseptic, probably possesses no advantage over other salicylates (*v. s.*).

Division III.—Boric Acid

Boric Acid.—This drug is a very valuable urinary antiseptic which is not yet sufficiently appreciated, for it possesses the power of acting equally well in an acid or an alkaline urine, so that while inferior to urotropin, or even the benzoates, in an acid urine, it is almost the only effective drug in cases where the urine is ammoniacal. Large doses must be given to get a sufficient effect, and these must be carefully watched, as the substance is fairly poisonous when given in sufficient quantities. Most people will readily tolerate 60 gr. in a day for a short time; more than this should never be given to begin with.

The Essential Oils and Resins

Sandalwood Oil and its Derivatives; Copaiba; Cubebs.

These drugs have long been employed in the treatment of gonorrhœa, and their efficacy in this disease seems beyond dispute. The first named has very largely replaced the two older drugs, owing to the fact that it is at least as efficient, and it is much less likely to produce toxic symptoms.

As to whether these substances ought to be regarded as antiseptic there is some dispute. Some writers speak of them rather as sedatives and astringents, but there is evidence that they do possess a true antiseptic action, and that this is exerted more against the pyogenic cocci than other organisms. Sandalwood oil is a good and effective drug to give in cystitis due to pyogenic cocci with ammoniacal urine containing pus.

Certain derivatives of oil of sandalwood are sold under the name of santyl, gonosan, etc. Santyl is santalol salicylate, santalol being one of the substances contained in the oil. It is pleasanter to take than the crude oil.

Uva Ursi and Arbutin.—Uva ursi folia in the form of an infusion has long been used as a diuretic and urinary antiseptic. It has a slight but noticeable diuretic action. As an antiseptic it is not of very high repute, but experimental evidence goes to show that it is of value, having a good all-round antiseptic action and being especially efficient against B. coli. Uva ursi contains amongst other substances an essential oil and a crystalline glucoside arbutin. Arbutin gives rise to the excretion of hydroquinone in the urine, which turns dark-brown or black after some hours' exposure to the air. Arbutin alone has been used as a urinary antiseptic under the impression that it is the active principle—this is not the case; its action is decidedly inferior to that of an equivalent amount of uva ursi.

Buchu Folia is given as an infusion for the same purposes as uva ursi. The action of buchu is probably somewhat similar, though it contains no such substance as arbutin. It is generally given as much for its diuretic action as for its antiseptic properties, and is rather

more popular than uva ursi though possibly not so effective.

Agropyrum (B.P.), *Triticum* (U.S.P.). Couch Grass.

Decoctum Agropyri (B.P.).
Dose : ½–2 fl. oz. (15–60 ml.).

Extractum Agropyri Liquidum (B.P.). Fluidextractum Tritici (U.S.P.).
Dose : 1–2 fl. dr. (4–8 ml.).

The preparations of this substance have been given as diuretics and urinary antiseptics.

The Application of the Pharmacology of the Urinary Antiseptics to Therapeutics

A very brief outline will now be given of what, based upon what is known experimentally as to the action of these drugs, are, in the opinion of the author, legitimate deductions as to their practical application to treatment.

The use of any given urinary antiseptic will depend upon (1) whether the urine is acid or alkaline; (2) the organism which is infecting the urinary tract.

For all organisms when the urine is, or can be made, highly acid, the most effective drug is hexamethylenetetramine (Hexamine, B.P., or Urotropin). As the power of this drug depends solely upon the formation of formaldehyde in the urine, and this latter varies with the acidity, it follows that when giving it acid sodium phosphate should usually be given as well, and that to give citrates, etc., with it is simply to inhibit its action.

Since this drug alone is sufficiently powerful completely to prevent the growth of bacteria in the urine (when the acidity of the latter is high enough), it is always used as a prophylactic before operations, catheterisation, etc.

When the urine is alkaline and undergoing ammoniacal fermentation, if the condition, as is usually the case, is due to a mixed infection of putrefactive organisms, the best drug to use is boric acid in as large doses as possible. Uva ursi may also be given in conjunction, and should it be desired to try the effect of rendering the urine alkaline in B. coli infections, these two drugs in combination with citrates are the ones to give, while urotropin (for the reasons given above) should not be given with the citrates.

Lastly, when the urine is alkaline or ammoniacal from a pure infection with the staphylococcus, sandalwood oil is a very useful drug.

A. R. J.

THE DIGITALIS SERIES

Introduction

The digitalis series embraces a large number of drugs which are characterised by a common action upon the heart. The drugs have very diverse origins and histories; squill was used for hundreds of years as an emetic before its cardiac action was recognised; strophanthin and antiarin were both discovered owing to their use in Africa and Borneo as arrow poisons, and bufagen is derived from the poison glands of toads; digitalis, the most useful of all the series, was introduced into medicine by Withering in 1785.

The active principles of the crude drugs in all cases have been found to be either glucosides or bodies closely allied to glucosides, but this is the only chemical or physical property common to the series, and in all other respects the glucosides show the widest divergence and are included together in one group, not on account of their chemical resemblance, but on account of their common action upon the heart. For convenience the whole group may be included under the term "cardiac glucosides."

Chemical Properties

Digitalis.—In 1874 Schmiedeberg showed that digitalis seeds contained at least three glucosides possessing a cardiac action, namely, digitoxin, digitalin and digitalëin, and also a saponin, digitonin, which had no cardiac action.

Kiliani and Cloetta have since investigated the question and have confirmed Schmiedeberg's conclusions in their main points; they have shown that the leaves contain, firstly, considerable quantities of digitoxin, a crystalline glucoside that is insoluble in water, but held in solution in water by digitonin, and one that has a very powerful action upon the heart; secondly, small quantities of digitalin, another glucoside insoluble in water; and thirdly, a considerable quantity of a third glucoside, which is soluble in water but which has a feebler cardiac action than digitoxin. This last glucoside was stated by Kiliani to be the same as the digitalëin isolated by Schmiedeberg, but Cloetta stated that it was different from digitalëin and called it soluble digitoxin, and has placed it upon the market as "digalen."

The action of tincture of digitalis depends chiefly upon its content of digitoxin, but it is modified by the presence of the other glucosides. Unfortunately different tinctures vary greatly in strength (differences of 400 per cent. have been observed); the preparation will only keep about twelve months, and after this time loses strength, and also it is unsuitable for injection. Great efforts, therefore, have been made to isolate from digitalis a pure active principle, free from these objectionable properties, and a very large number of preparations have been placed upon the market. Dixon has summarised the evidence concerning a large number

of these preparations and gives the following table of their chemical relations—

TABLE I.

Glucosides of Digitalis folia, with their synonyms.

Digitoxin, insol. in water, sol. in chloroform	Digitaline crystallisée (Nativelle). Not quite pure. Digitaline cryst. chloroform (French Codex). Digitaline amorph. (Homolle). Variable in composition. Digitoxin (Merck).
Digitalin, insol. in water and only slightly sol. in chloroform	Digitalinum pulv. pur. (German). Mixture of digitonin and digitaline. Digitalëine (Nativelle). Digitalinum Verum (Kiliani). Digitaline Amorph. (French Codex).
Digitonin, sol. in water.	Digitalëine (Houdas). Digitalinum Verum (German Pharm.).

The compositions of the above substances are fairly well established, but the compositions of the following are extremely doubtful.

Digitalëin, sol. in water, insol. in chloroform	Digitoxin (Keller). Gitalin (Kraft)? Digalen (Cloetta)?

The following preparations are said to contain a mixture of all the active principles—

Digipuratum—the residue left after extraction of the leaves with alcohol and ether.

Digitalone—a preparation of the water-soluble constituents of digitalis.

The pharmacological action of these different preparations will be considered later.

Strophanthus.—The sole official source of the pharmacopœial strophanthus preparations is the seeds of Strophanthus Kombé; unfortunately the supply of these is extremely irregular, and most strophanthus preparations are now made from the seeds of Strophanthus Hispidus. From both of these sources glucosides closely resembling each other are isolated, and are termed Kombé Strophanthin and Hispidus Strophanthin; these are amorphous bodies, fairly stable and freely soluble in water.

Distinct from these is the crystalline product obtained from Strophanthus gratus, which is often called Gratus Strophanthin, but which is better termed Ouabain.

From nearly all the other members of the digitalis series bodies resembling glucosides have been isolated in varying degrees of purity: Scillain (obtained from Scilla maritima), Helleborein and Helleborin (Helleborus niger), Convallamarin (Convallaria), Adonidin (Adonis), Oleandrin, Nerin and Neriodorin (Nerium), Euonymin (Euonymus), Antiarin (Antiaris), Thevetin and Cerberin (Thevetia), Cheiranthin (Cheiranthus), Coronillin (Coronilla), Tanghinin (Tanghinia venerifera), and Apocynein (Apocynum), which are all glucosides, while Apocynin (Apocynum) is indifferent, and Erythrophlœine (Erythrophlœum guinense) is a glucosidal alkaloid. Bufotalin, Bufonin and Bufagen, the bodies isolated from toads, appear to be related to cholesterin.

Pharmacological Action of Cardiac Glucosides

The action of these drugs upon the heart is by far their most important action. In addition they have the following common properties, they are powerful local irritants, they are in part broken down in the alimentary canal and are absorbed slowly, they stimulate the lower centres of the brain, and they produce cumulative poisoning. These latter properties are for the most part highly undesirable if the drug is desired to act upon the heart, and hence a knowledge of them is necessary in order to select the best drug for therapeutic use. For example, the irritant action upon the alimentary canal is so strong in the case of some members of the series that the drugs are used as drastic purges or emetics, and not as cardiac remedies.

Cardiac Action.—This action is of such great importance that it deserves to be considered first, for the other actions of these drugs are chiefly important because of the difficulties they cause in administering the drug in a satisfactory manner.

Action upon the Frog's Heart.—Boehm in 1872 described the action of digitalis upon the intact frog, and later workers have confirmed his conclusions. The first effect is a slowing of the rhythm of the heart; this is followed by a stage in which the systole is more complete and the diastole less complete, and at about the same time heart block usually appears, the ventricle contracting after every alternate auricular contraction. Finally, diastole becomes still more imperfect and the ventricle is arrested in systole, while the auricles continue to beat for some time after. If a large dose of digitalis is given, the heart contracts into systole without the appearance of block, but if a very small dose is given heart block appears and will continue for some days without the occurrence of systole (Straub); with small doses the heart is sometimes found to be arrested in diastole. It is obvious from these facts that the action of the digitalis glucosides upon the frog's heart is very complicated, and attempts have been made to elucidate it by a study of the excised organ.

Unfortunately most experiments with isolated frog's hearts have been carried out with unsatisfactory technique, and very contradictory results have been obtained. The following conclusions are drawn chiefly from observations upon the isolated frog's heart by Straub, who

used strophanthin, and by the writer, who used digitoxin and strophanthin.

If a moderate dose of a glucoside be given, sufficient to kill the heart in about one hour, (for example, a fluid containing 0·001 mg. strophanthin per c.c.), the following alterations are observed—

(1) *First or Therapeutic Stage.*—An increase in the amplitude of the heart's beat occurs almost at once and is associated with an increase in volume output; this effect, however, is scarcely noticeable in the fresh heart, but is very well marked in the tired heart; but both in the fresh and the hypodynamic heart a well-marked increase in the strength of the auricular contraction is observed. Straub shows that this stage is associated with a slight decrease in diastolic relaxation, an increase in systolic contraction, and a slight increase in the irritability of the heart. The rate of the contraction from auricle to ventricle is not altered. During this stage the output per beat and per minute is increased.

(2) *Second or Toxic Stage.*—This occurs in about twenty minutes and is marked by a decrease in the amplitude of the heart's beat, the diastolic relaxation is increased, the systolic contraction is diminished, the excitability of the ventricle is decreased, and the rate of conduction steadily decreases. The output per beat and per minute is decreased. During this stage the impairment of conduction between the auricle and ventricle usually produces heart block, and halved rhythm ensues. Owing to the ordinary laws of heart action the diminution in the frequency of the beat causes an increase in the force of each beat, but the total output per minute is not so great as in stage 1. This stage has led to much confusion, as it has often been described without recognising the occurrence of heart block, and hence the cardiac glucosides have been stated to cause a marked diminution in the rate of the heart and a very great increase in the strength of the beat. If the sinus rate of an excised heart be observed, little alteration in its rate can be determined as a result of the action of cardiac glucosides until the heart is almost dead.

(3) *Third or Final Stage.*—The third stage is marked by the death of the ventricle, which may die either in systole or diastole.

The final condition is determined by numerous factors; systole always occurs with strong concentrations of the drug, and diastole often occurs with very weak concentrations. A fresh heart tends to die in systole and an exhausted heart in diastole. Excess of alkali or calcium, or presence of serum in the perfusion fluid, usually produce systole (Werschinin). If the fluid is faintly acid or contains less calcium than normal, diastole always occurs.

It appears, indeed, that the cardiac glucosides have two distinct toxic actions—they decrease the rate of conduction and increase the systolic tone; if the first action predominates diastolic arrest occurs, if the second predominates systolic arrest occurs. The occurrence of systolic arrest in the frog's heart is of no therapeutic importance, for it does not occur in mammals. It forms, however, a convenient sign by which a cardiac glucoside may be recognised, and this is of importance in the standardisation of the cardiac glucosides.

Action on Mammalian Heart.—Three stages are recognised in the action of the drug. In the first or therapeutic stage the heart is slowed owing to a central stimulation of the vagus, the ventricles empty themselves more completely than formerly, diastole may be diminished, but is sometimes increased, and the output of the heart per beat is usually increased.

In the excised mammalian heart, if the heart is beating with a feeble, irregular beat, the force of the beat is greatly increased and the beat becomes more regular. The output per minute in this stage is increased.

In the second stage the rhythm of the ventricle becomes very slow, and the auricle and ventricle often beat with independent rhythms owing to heart block being established. The auricular beat is weaker than in the first stage and the ventricular beat is of about the same strength. Owing, however, to the slowing of the ventricular rhythm the output per minute is decreased. The most marked feature of this stage is, as in the frog, interference with conduction, producing heart block.

The third stage consists of delirium cordis, the ventricle beats rapidly and irregularly, and there is auriculo-ventricular arrhythmia.

The ventricle finally passes into fibrillary contraction and dies in diastole.

The three stages observed in the action of digitalis on the mammalian heart correspond fairly closely to the three stages in the frog's heart.

Action on the Peripheral Vessels.—In sufficiently large doses all the digitalis glucosides produce vaso-constriction, but the vaso-constrictor effect is much more marked with digitoxin than with strophanthin. In both cases however, the concentration required to produce definite vaso-constriction in isolated tissues is much larger than that required to kill the isolated heart. If a lethal dose of strophanthin is injected into an intact animal, it does not kill the heart at once, and a peripheral vaso-constrictor action is noted, and since this is associated at first with an increased cardiac output there is a well-marked rise in the blood pressure, which continues until the heart passes into the second stage of poisoning. This action

is not of therapeutic importance, for a sublethal dose, sufficient to affect the heart of a mammal, does not produce marked vaso-constriction. In man, moreover, no rise in blood pressure can be demonstrated after the therapeutic administration of cardiac glucosides.

Action on Renal Secretion.—When cardiac glucosides are administered to patients suffering from cardiac disease and œdema, their administration is followed by a well-marked increase in the urinary secretion. If digitalis is administered to a normal animal there is a very slight increase in the amount of urine secreted, and even this slight increase is denied by some observers. The action of cardiac glucosides upon the kidney vessels has been observed by Gottlieb and Magnus and Katzenstein; large doses are found to produce vaso-constriction in the kidney as in the other organs of the body, but Katzenstein shows that a higher concentration is required to produce vaso-constriction in the kidney than in the other organs.

The most probable explanation of the increase in the urinary secretion in healthy animals is that the increase in cardiac output increases the blood flow through the kidneys, and that the vaso-constrictor effect never occurs with therapeutic doses. The cardiac glucosides are partly excreted through the kidneys and may produce some diuresis by irritation of the kidney epithelium.

There is no doubt, however, that the increase in renal secretion observed when the drugs are administered to patients suffering from heart disease is due chiefly, if not entirely, to increase in the cardiac output.

Action on Alimentary Canal.—All the digitalis glucosides act as irritants to the intestinal epithelium, and tend to produce vomiting and purgation. This action is well marked in the cases of squills, which is used as an emetic, and of euonymus, which is used as a purgative.

The cardiac glucosides have no action upon the isolated gut in concentrations far higher than those required to kill the isolated heart.

The digitalis glucosides have practically no action on striped muscle, and very little action upon plain muscle; their action upon the heart muscle is, therefore, a very striking example of the selective action of drugs.

Local Action.—An intense local irritation is produced when diluted tincture of digitalis is injected hypodermically, and when given by mouth it often produces irritation of epithelium of the stomach and intestines. This effect has been investigated with a view to finding some preparation which will not produce it and that can be given both hypodermically without producing local irritation, and by mouth without the risk of producing vomiting.

The irritant action varies greatly in different members of the series. Digitoxin is intensely irritant, and so is the saponin digitonin; digalen and digipuratum are as strongly irritant as tincture of digitalis; digitalone, it is true, is not irritant, but this preparation has a very feeble cardiac action (Cow); Dixon concludes that "no active preparation of digitalis is yet known which can be injected under the skin without causing more or less pain and inflammation. Strophanthin is less irritant than digitoxin, but it also produces irritation on hypodermic injection. Squills and euonymus are, as already mentioned, intensely irritant.

The glucosides also act as local anæsthetics, and strophanthin, ouabain and erythrophlœine have been recommended as local anæsthetics for the eye, but their irritant action precludes their use for this purpose.

Action on Central Nervous System.—In large doses cardiac glucosides stimulate the lower centres of the brain, and produce stimulation of the vagus, which causes slowing of the heart and vomiting. The vomiting is observed regularly when large doses of the glucosides are injected into animals. The slowing of the heart observed when cardiac glucosides are given to healthy animals is probably entirely due to central stimulation of the vagus.

Absorption of Cardiac Glucosides

From the facts mentioned it is obvious that the condition determining the absorption of cardiac glucosides are of the highest therapeutic importance. When given by mouth these drugs may produce vomiting due to local irritation, and when they enter the gut their absorption is hindered by their purgative action. Moreover, the active principles of digitalis are insoluble in water, and are only kept in suspension by the digitonin present, and this also hinders their absorption. Finally, it has been shown that many of these glucosides are destroyed by the ferments of the gut.

These facts show how uncertain is the absorption of these bodies and explain the marked differences observed between the relative strengths of certain preparations as determined by injection, and the results obtained in therapeutics, when they are administered by mouth. For example, tincture of strophanthus, when injected or tested upon an isolated heart, is found to have the same action on the heart as tincture of digitalis, but to be more than forty times as strong; but therapeutic experience shows that the former is not nearly as efficient as the latter, when the drugs are given by mouth. Undoubtedly the reason for this is that strophanthin is not absorbed as readily as the digitalis glucosides. Hatcher has investigated the absorption of ouabain in cats and has shown that the rate of absorption varies enormously

in different animals; moreover, the mode of administration is of great importance, for he found that administration of ouabain in concentrated solution in alcohol greatly increased the rate of absorption. He also found that animals in a poor state of health absorbed less ouabain than healthy animals.

These results show clearly that the standardisation of these drugs by injection into animals has certain well-defined limits of usefulness, for while two samples of the same preparation can be accurately compared by injection into animals, nevertheless the method will not always serve to determine the relative therapeutic values of two different glucosides.

Excretion of Cardiac Glucosides

Hatcher showed that the glucosides were not destroyed in the body, but that when injected they were excreted in part by the kidneys, and in part (66 per cent.) by the fæces; the excretion by the kidneys began a few hours after injection, and nearly all of the drug was excreted within twenty-four hours.

Cumulative Action

All of the cardiac glucosides have a well-marked cumulative action, but the cause for this is unknown. Hatcher's experiments upon the absorption of ouabain suggested that the cumulative action observed in therapeutics may be due to alterations in the rate of absorption, for if administration of the drug improves the efficiency of the circulation, the absorption of the drug will be increased, and an increased quantity of the glucoside enters the blood stream. Fraenkel, however, found that some cumulative effects were observed when digitoxin was given subcutaneously, and therefore a true cumulative action upon the tissues must exist.

The writer found that there was no evidence that isolated tissues could retain strophanthin when this drug was perfused through them. The reason of the cumulative action is therefore unknown; but there is no satisfactory evidence for the existence of any cardiac glucoside that can act upon the heart and yet not produce a cumulative action.

Standardisation of Digitalis

As already mentioned, the strength of tinctures of digitalis obtained from different sources varies enormously. The strength of the tincture depends upon the source of the leaves, the season at which they were plucked, the method by which they were dried, the technique employed in making the tincture, and the age of the tincture. Some form of standardisation is therefore essential. Unfortunately the most important preparation of the whole series, tincture of digitalis, depends for its action upon a mixture of different glucosides, and it is impossible to extract all of these quantitatively; chemical standardisation is therefore impossible in this case and is very difficult in the case of the crude preparations of the other drugs.

Standardisation upon animals is therefore necessary. The chief objection to the various methods used is that they all depend upon results obtained by injecting drugs, and, therefore, the results do not indicate the relative potency of different drugs when given by mouth, because, as already mentioned, the potency of the drugs is modified to a large extent by their rate of absorption and the degree in which they are destroyed in the alimentary canal. This objection does not apply, however, when the strengths of different samples of the same drug are compared, as, for example, different samples of tincture of digitalis, and for this last purpose the standardisation of the drug upon animals yields very satisfactory results.

Digitalis preparations can be standardised by the following methods—

1. By determining the amount required to produce a standard effect on a frog when injected hypodermically.
2. By determining the concentration required to kill an isolated frog's heart.
3. By determining the amount required to kill a cat when given intravenously (Hatcher).

The first of these methods is the only one likely to prove suitable for general application, and it is extremely simple. A series of frogs are weighed, each is injected with a known quantity of the drug to be tested and the quantity of drug determined that will produce a definite effect within a certain time. Different observers recommend different "end points," but the writer has found the most satisfactory method to be to kill all the frogs at the end of two hours and determine the smallest quantity of drug that has produced systolic arrest of the ventricle within this time in a 20 gm. frog. The only difficulty in the method is that a frog may live two to three hours after the heart is arrested in systole, and there is no convenient way of determining whether the heart is in systole without killing the frog. As already observed, this method does not allow a determination of the relative therapeutic efficiency of two different glucosides (*e. g.* tincture of digitalis and tincture of strophanthus), but it yields very accurate information as to the relative therapeutic efficiency of two samples of the same drug.

Therapeutic Application of Digitalis

The therapeutic action of digitalis is practically confined to its action upon the heart,

and Mackenzie has shown that by far the most marked beneficial results are obtained with this drug in cases of auricular fibrillation. Mackenzie and Cushny studied the action of the drug in these cases and showed that the effect produced was to slow the rate of ventricular contraction and cause the ventricle to beat with a slower, more powerful, and more efficient beat. It was long uncertain whether the cause of the slowing of the heart rate in cases of heart disease was due to a direct action of digitalis on the ventricle of the heart, or due to central stimulation of the vagus centre. Cushny, however, has shown that "the reduction in the rate of the pulse under digitalis is largely, though not exclusively, inhibitory in origin in non-fibrillating cases of heart disease, but in cases of auricular fibrillation increased inhibition seems to play no part in the slowing of the pulse."

The exact cause of the decrease in the rate of the heart in auricular fibrillation appears uncertain. The most obvious suggestion is that the drug acts upon the bundle of His, and thus prevents conduction from the auricle to the ventricle. But the therapeutic effect of digitalis undoubtedly corresponds to the first stage of digitalis poisoning in either the frog or the mammal, and at this stage in neither animal is there any impairment of conduction between the auricle and ventricle.

Another possibility is that the drug decreases the excitability of the ventricle; and although the excitability of the frog's ventricle increases slightly in the first stage of poisoning, yet Cushny found that the excitability of the mammalian ventricle decreases slightly. The evidence, however, is very slight, and the most probable view appears to be that the chief action of digitalis upon the diseased heart is to increase the strength of contraction of the ventricle, in the same manner as it increases the strength of the contraction of the "hypodynamic" excised heart of the frog and of the mammal. This improved contraction augments the flow of blood through the coronary arteries and thus improves the condition of the heart. There is no direct evidence that improvement in the nutrition of the mammalian heart decreases the excitability of the ventricle, but it is a well-known fact that rest in bed, without any drugs, will decrease the rate of the heart in patients with heart disease, and this suggests the possibility that improved nutrition of a diseased heart may produce slowing of the ventricle.

The Pharmacological Value of the Different Preparations of Digitalis

Different observers have obtained extraordinarily contradictory results when investigating the pharmacological action of the different isolated glucosides of the digitalis series. The following table shows some of the values obtained by injections into frogs.

TABLE II.

Preparation.	Dose required to produce systolic arrest of the heart of a 20 gm. frog in one hour.	Observer.
Tincture of Digitalis	0·1 c.c.	Hatcher.
,, ,,	0·15 c.c.	Cow.
Digitoxin	0·17 mg.	Famulener and Lyons.
Digitalëin	0·5 mg.	Famulener and Lyons.
Digalen	0·44 mg.	Hatcher.
Digipuratum	2 mg.	Hatcher.
Strophanthin (Burroughs & Wellcome)	0·02 mg.	Clark.
Ouabain	0·01 mg.	Famulener and Lyons.
Digitalone	over 0·3 c.c.	Cow.

There is a general agreement that digitoxin is the most potent of all the glucosides present in digitalis leaves, but it is highly irritant and very insoluble. Digalen, according to Hatcher and Cow, has a feeble pharmacological action and is very irritant; it has, therefore, little or no advantage over tincture of digitalis. Digitalone is not irritant, but has a very feeble pharmacological action. Cow concludes that neither digalen, digitalone nor digipuratum shows any marked superiority over tincture of digitalis.

Strophanthin

The pharmacological action of strophanthus upon the heart appears to be identical with that of digitalis, and when either the tincture or the isolated glucoside is tested upon isolated tissues or by injection into intact animals, the same results are obtained as with corresponding preparations of digitalis, the chief difference being the far greater strength of the strophanthin preparations.

Clinical observation shows, however, that administration of strophanthin by mouth is not nearly as efficient in heart disease as administration of digitalis. The reason for this must be either that not so much strophanthin is absorbed as digitalis, or that strophanthus is excreted more rapidly than it is absorbed, but the latter alternative is very improbable, for cumulative poisoning can be produced with strophanthus.

Strophanthin differs from digitoxin in that it is soluble in water, is less irritant, and has less vaso-constrictor action.

Intravenous Administration of Strophanthin.—Owing to its solubility in water strophanthin is more suitable for intravenous administration

than digitalis. Fraenkel first employed this method, and recently it has been employed in England by various workers.

A dose of 0·7 to 0·3 mg. ($\frac{1}{100}$ to $\frac{1}{250}$ gr.) is given in one dose, and the dose may be repeated after twenty-four hours. The drug acts on the heart in the same manner as digitalis when given by mouth, but it causes slowing of the pulse in as short a time as ten minutes. The effects last several days.

This method of administration is of great use when it is desired to produce a rapid effect upon the heart, or when digitalis by mouth produces vomiting.

The chief use of intravenous strophanthin is in cases of auricular fibrillation, but it appears that it might prove of value in some cases of collapse; but to attempt to reduce the rate of the heart in fever by administration of cardiac glucosides is, of course, futile.

Squills

The action of squills upon the isolated heart is similar to that of digitalis, but tincture of squills has a stronger action that tincture of digitalis. Squills also produces more marked vaso-constriction than digitalis. The local irritant effect of squills is similar to that of digitalis.

In therapeutics squills is given as an expectorant or an emetic on account of its local irritant action. When given by mouth squills does not have as strong an action on the heart in cases of auricular fibrillation as has digitalis, and this is possibly due to imperfect absorption of the drug. Squills has a more marked diuretic action than digitalis, but the cause of this is not known.

The remaining drugs included in the series of cardiac glucosides all have less action upon the heart than digitalis, and are of little importance in cardiac therapy.

Materia Medica

The preparations enclosed in brackets are of little therapeutic importance.

Preparations of Digitalis

1. Digitalis Folia (B.P.). Digitalis (U.S.P.). $\frac{1}{2}$–2 gr. (3–12 cg.). The leaves should be gathered from plants commencing to flower. The dried leaves lose about 50 per cent. of their strength after keeping for one year.
2. (Extractum Digitalis (U.S.P.). $\frac{1}{5}$ gr., 10 mg.).
3. (Fluidextractum Digitalis (U.S.P.). 1 min., 5 cl.).
4. Infusum Digitalis (B.P., U.S.P.). 2–4 fl. dr. (8–16 ml.). This preparation contains all the active principles of digitalis, and is used extensively on the Continent. It loses strength rapidly on keeping, and freshly made preparations should always be used.
5. (Infusum Digitalis Concentratum (B.P.C.). 15–30 min. (1–2 ml.). This preparation deteriorates rapidly on keeping.)
6. Pilulæ Digitalis Compositæ (B.P.C.). Each pill contains 1 gr. each of digitalis, squill and mercury pill.
   Dose: 1–2 pills.
7. (Pilulæ Digitalis et Opii Compositæ. B.P.C.).
8. (Succus Digitalis (B.P.C.). 5–10 min., 3–6 dl.).
9. Tinctura Digitalis (B.P., U.S.P.). 5–15 min. (3–10 dl.). Different samples vary greatly in strength, and therefore the preparation should be standardised. Under favourable conditions the preparation will preserve its strength unaltered for one year.

Preparations of Digitalis Glucosides

Digitalinum (B.P.C.). $\frac{1}{32}-\frac{1}{4}$ gr. (2–15 mg.).
Digitalinum Pulverisatum Purum. $\frac{1}{32}-\frac{1}{4}$ gr.
Digitoxinum (B.P.C.). $\frac{1}{250}-\frac{1}{64}$ gr. ($\frac{1}{4}$–1 mg.).

Other Commercial Preparations

Nativelle's Digitaline Granules. $\frac{1}{240}$ gr. ($\frac{1}{4}$ mg.).
Digalen (Cloetta). 5–15 min. (3–10 dl.).
Digipuratum. In tablets or ampoules.
Digitalone. 15 min. (1 ml.).

The merits of these preparations have been discussed in the preceding paper. All active preparations of digitalis glucosides produce irritation when injected hypodermically. When given by mouth none of these drugs show any certain superiority over a standardised Tincture of Digitalis.

Preparations of Strophanthus

1. Strophanthus. From the seeds of S. Hispidus.
2. Strophanthi Semina (B.P., U.S.P.). From the seeds of S. Kombé.
3. (Extractum Strophanthi (B.P.). $\frac{1}{4}$–1 gr., 16–60 mg.).
4. Tinctura Strophanthi (B.P.). 2–5 min. (12–30 cl.). *Four times stronger than that of B.P. 1898.* Should always be standardised, as strength varies. When given by mouth it does not produce as satisfactory therapeutic cardiac effects as Tinct. Digitalis.
5. Tinctura Strophanthi (U.S.P.). 8 min. (5 dl.).
6. Strophanthinum $\frac{1}{300}-\frac{1}{100}$ gr. 0·2–0·6 mg. (From S. Hispidus).
7. Strophanthinum (U.S.P.). $\frac{1}{300}-\frac{1}{60}$ gr. (0·2–1 mg.) (from S. Kombé). This preparation can be given intramuscularly or intravenously, and produces satisfactory therapeutic cardiac effects.

Other Preparations

8. Ouabain (Crystalline Strophanthin gratus of Thoms). This is a crystalline body of known chemical composition. It has the same therapeutic action as No. 7.

Preparations of Squills

1. Scilla (B.P., U.S.P.). 1–3 gr. (6–20 cg.).
2. Acetum Scillæ (B.P., U.S.P.). 5–15 min. (3–10 dl.).
3. Oxymel Scillæ (B.P.). ½–1 fl. dr. (2–4 ml.).
4. Syrupus Scillæ (B.P., U.S.P.). ½–1 fl. dr. (2–4 ml.).
5. Pilula Ipecacuanhæ cum Scilla (B.P.). 4–8 gr. (25–50 cg.).
6. Pilula Scillæ Composita (B.P.). 4–8 gr. (25–50 cg.).
7. Tinctura Scillæ (B.P., U.S.P.). 5–15 min. (3–10 dl.).

The tincture is the only preparation commonly used in cardiac therapy, the others being used as expectorants. Tincture of squills is inferior to tincture of digitalis in cardiac disease.

Urginea is the official substitute for squill in India and the Eastern Colonies.

Preparations

1. Urginea (B.P.). 1–3 gr. (6–20 cg.).
2. Acetum Urginea (B.P.). 5–15 min. (3–10 dl.).
3. Oxymel Urginea (B.P.). ½–1 fl. dr. (2–4 ml.).
4. Syrupus Urginea (B.P.). ½–1 fl. dr. (2–4 ml.).
5. Pilula Ipecacuanhæ cum Urginea (B.P.). 4–8 gr. (25–50 cg.).
6. Pilula Urgineæ Composita (B.P.). 4–8 gr. (25–50 cg.).
7. Tinctura Urginea (B.P.). 5–15 min. (3–10 dl.).

The tincture is the only preparation commonly used in cardiac therapy, the others being used as expectorants. Tincture of squills is inferior to tincture of digitalis in cardiac disease.

Other Drugs containing Cardiac Glucosides are—

Apocynum, Convallaria, Euonymus, Helleborus. There is no evidence that any of them are of equal value to digitalis in cardiac therapy.

A. J. C.

ACONITE, CEVADILLA AND STAVESACRE

The three medicinal substances in this group have been long used in the treatment of disease, but, as they differed considerably from each other in their therapeutic application, they were not considered to be in any way related to each other. The first was used as an antipyretic and cardiac depressant, the second as a local analgesic and a purgative, and the third as a parasiticide. The occurrence of poisoning from overdoses or accidental administration of the first two conferred on them a superior degree of importance, and, therefore, a larger number of, and much more minute, investigations have been undertaken into their composition and mode of action than has been the case with the third. Research has elicited such general similarities between the chemical characters of their active principles and the pharmacological actions exerted by them that they may be considered together.

They all contain alkaloids, somewhat unstable and difficult to obtain in a condition of purity; all of them to a greater or less degree act as protoplasmic poisons, and affect the nervous and, to a less extent, the muscular structures. Locally applied, they cause peripheral irritation without marked inflammation, followed by persistent local anæsthesia, and after absorption they paralyse respiration, lower the temperature, and affect the circulation by diminishing the rate of the cardiac contractions.

Aconite.—The official source of the alkaloid aconitina is the dried, short, conical root of the Aconitum Napellus (*Ranunculaceæ*), called Monkshood from the shape of its blue flowers. The roots are dark brown, marked with the white scars of broken rootlets. Internally a large whitish, seven-angled pith is characteristic. There is no odour or taste, but a peculiar persistent tingling, followed by numbness, is experienced when a minute fragment is chewed. Tinctura Aconiti (B.P., U.S.P.) contains 0·04 per cent. of alkaloids, and is twice as strong as the B.P. 1898 tincture. The dose of the tincture is from 2 to 5 min. (12–30 cl.) for repeated administration, but the effects of the larger dose must be carefully observed to guard against the possibility of collapse. Linimentum Aconiti (B.P.) contains 0·2 per cent. of alkaloids with camphor in 90 per cent. alcohol. Fluidextractum Aconiti (U.S.P.) is ten times the strength (0·4 per cent.) of the tincture; its average dose is 1 min. (5 cl.).

The international tincture must contain ·05 per cent. of alkaloids. There are several stronger tinctures, which however intensify the danger of an overdose; some liniments compounded with belladonna in addition, and combinations with or solutions in, chloroform. This last solvent penetrates the skin rapidly and thus aids the local action.

Composition.—Aconitina (B.P., U.S.P.—the only official alkaloid) is a base first isolated in 1833. It is very sparingly soluble in water, occurring in hexagonal prisms of the rhombic order, colourless, with a melting point of 198° C. Above this it decomposes and acetic acid is produced. It can undergo hydrolysis with the production of benzaconine, and it may be considered as acetyl-benzaconine, $C_{24}H_{37}.CH_3CO.C_6H_5CO.NO_{10}$ or $C_{33}H_{45}NO_{12}$. It is very soluble in alcohol, the solution being dextro-rotatory, and, in the strength of 1 in 10,000, one drop gives the characteristic physiological effect on the tongue. It is also soluble in chloroform. Potassium permanganate solution precipitates purplish-red crystals from dilute solutions of aconitine (1 in 4000) acidified faintly (acetic acid). Unguentum Aconitinæ (B.P.) 2 per cent. with oleic acid and lard is the official preparation. Chloroformum Aconitinæ (B.P.C.) is a 0·23 per cent. solution in chloroform.

Benzaconine, $C_{24}H_{37}.H.C_6H_5CO.NO_{10}$, first isolated in 1857 as "Napelline," is amorphous and very bitter, but does not give the physiological test. It is sparingly soluble in water, and can be decomposed into benzoic acid and aconine. Aconine, $C_{24}H_{37}.H.H.NO_{10}$, is amorphous, sweet, readily soluble in water, and toxic. Aconitic acid also occurs, but is non-toxic.

The alkaloids which occur in other species of aconite are not identical with the above, and the most important of them is Pseudaconitine, obtained from Aconitum Ferox, used in Northern India as a poison for wild animals, and used on arrows in warfare.

Toxicity.—Aconitine is the most active, the dose for man being from $\frac{1}{640}$ to $\frac{1}{500}$ or $\frac{1}{400}$ gr. (or 0·1 to 0·15 mg.), benzaconine is about 200 times weaker, and aconine about 1800 times weaker than aconitine. (For minimum lethal dosage for cats, rabbits, guinea-pigs and frogs, *vide* Cash and Dunstan, *Trans. Roy. Soc.*, 1898).

Pharmacology.—When applied to the unbroken skin of man no effect is perceptible unless means are taken to aid aconitine to penetrate the epidermis, such as applying a solution in chloroform or applying the oleate ointment with friction. A watery solution will penetrate the skin of the foot of a pithed suspended frog and produce a peculiar irritation. No dilatation of vessels is observed nor destructive changes in the skin, but repeated movements, as if the foot were being touched and withdrawn. In man, tingling or burning sensations are experienced locally when the substance is absorbed, which are followed by numbness, thermal sensations being abolished more rapidly than tactile sensibility. These effects are caused by preliminary stimulation of the sensory nerve-endings, followed by paralysis, which lasts for a considerable time, possibly hours. When aconitine is injected subcutaneously, greater irritation is observed; in the frog the limbs are contorted and the animal may be motionless, or there may be spasmodic movements; in the rat the animal scratches the site of injection, and in man pain is complained of. Slight reddening and swelling of the skin has been observed in man when the ointment has been rubbed on a tender skin for a considerable time, this being the extent of any inflammatory reaction.

On mucous membranes the effects of sensory stimulation and paralysis are very manifest. When applied to the eyeball there is lacrimation and the eye is closed, when to the nostrils there is violent sneezing, and when to the mouth there is tingling in the tongue, lips and cheeks, with increased salivation. All these preliminary effects are succeeded by a degree of local anæsthesia. When swallowed, similar effects are produced on the palate, fauces, throat and stomach; a feeling of burning, of swollen tongue, constricted throat, nausea, vomiting and sometimes abdominal pain are complained of. Absorption takes place rapidly from the alimentary canal and from the subcutaneous tissues.

After absorption of a lethal quantity by a frog there may be observed irregular but violent movements, increased secretion from the skin, failure of respiration and some cardiac irregularity. Reflex excitability is impaired and lost before voluntary movements have ceased, and the heart continues to beat for a considerable time subsequent to respiratory paralysis. In a warm-blooded mammal, such as the rat, there is local uneasiness, slight restlessness, movements of the mouth indicating salivation, and a very transient quickening of respiration, followed by marked slowing. Respiratory difficulty becomes more pronounced, the rat rises on the hind limbs to aid the respirations, which are forced, and may be audible but slow; or it may remain in the normal posture with its respirations becoming slower and feebler, interrupted by spasmodic convulsions, which become more frequent, until death occurs from asphyxia. The cardiac impacts may be diminished in frequency and easily felt, or may be very rapid, irregular, and felt only with great difficulty. The temperature falls, and shortly before death there may be expulsion of urine. When respiratory failure occurs, the heart may still be observed to be beating, but not with sufficient regularity or force to support life. In animals which can vomit the exaggerated abdominal movements may be accompanied by emesis.

In man, constriction of the throat, nausea, vomiting, general tingling or burning sensations, dyspnœa, a weak and irregular pulse, together with a peculiar feeling of chilliness, are the most prominent symptoms. The temperature falls, and death is due to respiratory failure, though the irregularity and weakness of the cardiac contractions are very important factors in causing the fatal termination. There is not, as a rule, unconsciousness.

The respiratory function is thus powerfully affected by aconitine, at first acceleration and subsequent slowing being caused, leading to dyspnœa and asphyxia. It occurs whether the animal is anæsthetised or not, and whether the vagi are intact or severed. After death the phrenic nerve terminations are little impaired, and this evidence altogether seems to point to the main action being paralysis of the respiratory centre in the medulla oblongata. A respiratory stimulant, such as atropine, may retard the fatal result, as also does artificial respiration, but death subsequently occurs from cardiac paralysis.

Circulation.—In the frog, the heart, after a transient acceleration, is markedly slowed, and

may be arrested in diastole; and this arrest may be removed by atropine. It does not occur if the vagi are divided, and is, therefore, probably due to stimulation of the inhibitory vagal centre.

In mammals and in man, small doses diminish the rate and the contractile force, sometimes to a great degree. This is very noticeable where the heart is beating with excessive rapidity, as in conditions of pyrexia. When small lethal doses are administered a subsequent acceleration in the rate occurs, accompanied by irregularity and arrhythmia, with partial vagal paralysis; thus stimulation of the vagus at one time causes little or no effect, and at another causes restoration to a normal rhythm with consequent improvement in blood pressure. Later still, stimulation of the vagus produces no effect. The cardiac irregularity becomes greater. The auricles and ventricles are inco-ordinated, the ventricular contractions become fluttering, peristaltic, and quite inefficient. This series of effects is probably caused by poisoning of the cardiac muscle, and evidence is adduced for this view by the occurrence of very much the same train of symptoms in an isolated heart, which is without the nervous mechanism.

The blood-pressure falls during the period of slowly beating heart, and fluctuates during the succeeding stage of irregularity. It may be raised after poisoning when the inhibitory stimulation of the heart is prevented by vagal section. This points to a stimulation of the vasomotor centre. There appears to be little or no action on the peripheral circulation, and the somewhat complex effects may be summed up as caused by stimulation of the inhibitory centre, masking the stimulation of the vasomotor centre, and thus producing a slow heart and diminished blood-pressure. Then paralysis of the inhibitory mechanism, together with the weakening of the cardiac muscle and the paralysis of the vasomotor centre, cause rapid, irregular and feeble contractions of the heart and a fall in blood-pressure.

Central Nervous System.—The brain is not affected, apparently, consciousness being maintained till collapse occurs, and the motor centres remaining active, as evidenced by the asphyxial convulsive movements in the mammal and the persistence of voluntary movements in the frog. Nor is the spinal medulla powerfully affected, reflex movements being elicited till late in the poisoning, the diminution of reflex excitability observed in the frog being possibly due to diminished skin sensibility. The medullary centres are strongly affected, however, as mentioned above, and the marked fall in temperature, the feeling of chilliness occurring early and the vomiting are probably effects partly produced by stimulation of the respective nerve centres. The occurrence of slight convulsive movements in the rat before profound asphyxia, and the occurrence of similar movements in the non-asphyxiated frog, point to a slight stimulation of motor centres; this receives additional confirmation from the fact that the convulsions in mammals are not entirely abolished by artificial respiration.

The stimulation of the afferent nerves and their subsequent paralysis, which are striking features of aconite poisoning, occur whether the poison is locally applied or acts through the circulation. The occurrence of fibrillary twitchings in the muscles points to a similar, but much slighter, effect on the motor nerve-ends. These may still occur when the nerves are divided, but do not if they are curarised. That the stimulation of the sensory nerve-endings in the lungs explains the respiratory and cardiac effects of the poison has been advanced as a theory, but the progressive paralysis of the respiratory and other centres seems to be too profound to be altogether satisfactorily accounted for on this supposition.

Secretions.—There is not sufficient evidence of direct action on secretory glands. The occurrence of sweating may be explained by the venous state of the blood during asphyxia, and the salivation, lacrimation and the increase of nasal secretion may be accounted for by the peripheral sensory irritation.

Temperature.—Diminished circulatory and respiratory activity, with lowered blood pressure and asphyxial sweating, will obviously result in lowering the temperature. In a poisoned rat the temperature may fall 4° or 5° F. before death. The fall, however, begins sooner than can altogether be accounted for by these factors, and recovery from these conditions is not accompanied by an immediate rise in temperature. This, therefore, points to a depression of the central heat-regulating mechanism, which is not surprising when the marked depression of other vital centres is considered.

In pyrexia the high temperature can be effectively reduced by repetition of small doses.

Pupil.—The action on the pupil is uncertain. Some observers have reported a period of contraction, which undoubtedly occurs in the rat during poisoning, before the period of acute asphyxia. Others state that there is early dilatation of the pupil, which may be reduced by section of the cervical sympathetic. In any case, however, the pupil dilates during the later stages, and at death is widely dilated.

Metabolism.—Oxidation processes are diminished during administration of aconite directly as well as secondarily to depression of circulation and respiration.

Excretion.—Aconitine is excreted chiefly in the urine, but traces of it have been found in other secretions, such as the saliva, and in certain tissues (stomach and liver) when it has been admin-

istered hypodermically. Its elimination begins fairly rapidly, aconitine having been found in the urine four hours after administration. How rapidly the process is completed is not known.

Other Alkaloids.—It is sufficient to mention that *Benzaconine* acts on the circulation and on the respiration to a less extent, but in a similar manner to aconitine. It causes a fall of blood-pressure not removable by vagal section, and much later during the poisoning vagal paralysis. There is, on the other hand, conspicuous muscular weakness, and the motor nerve-ends are more strongly affected than they are by aconitine. The sensory nerve-ends are much less strongly affected in proportion.

Aconine antagonises the action of aconitine on the heart. The force of the heart is increased by it; and the irregularity produced by aconitine can be diminished by aconine. It paralyses the respiration by depressing the terminations of the phrenic nerve, and it acts on motor nerve-endings as curara does.

The action of the varieties of aconitines in other species of aconite differs in degree, rather than in kind, from that of ordinary aconitine. Thus pseudaconitine (Aconitum ferox) exerts a greater action on respiration and a slighter action on the heart than does aconitine. Fraser found it twice as lethal to rabbits but only one-sixth as lethal to frogs. Observations differ with regard to its relative toxicity, and it is doubtful if it has been obtained in a condition of purity.

Therapeutic Applications of Aconite.—These depend on the depressing actions on sensation and on the circulation. The liniment and the ointment are used to diminish pain in peripheral neuralgia, but the so-called ABC (Aconite, belladonna and chloroform) liniment is perhaps the most useful preparation for this purpose. Internally aconite is used to lower the blood-pressure, more especially when raised by excessive cardiac activity. In inflammatory conditions—such as tonsillitis, laryngitis and acute catarrh—it is a most useful remedy. It has also been used successfully in scarlet fever, acute gonorrhœa, and, combined with other diaphoretics, in acute rheumatism. The care required to be observed during its administration has tended to displace it in favour of less toxic antipyretic remedies.

Veratrine.—The source of veratrine is the dried ripe seeds obtained from the Schœnocaulon officinale or Asagræa officinalis. This is called cevadilla or sabadilla, and was formerly used medicinally. Veratrine (U.S.P.) is a mixture of several alkaloids: (1) veratrine, an amorphous grey powder, sparingly soluble in water (1 in 1560), soluble in chloroform, with formula $C_{37}H_{53}NO_{11}$; and can be decomposed into an aromatic acid, di-methyl-protocatechuic acid, $C_9H_{10}O_4$, and verin; (2) cevadine (also sometimes called veratrine), crystalline, and with formula $C_{32}H_{49}NO_9$, which can be decomposed into a fatty acid, α-methyl-crotonic acid, $C_5H_8O_2$; (3) cevadilline, amorphous, $C_{34}H_{53}NO_8$; (4) and others, as sabadine and sabadinine.

Veratrine (U.S.P.), $\frac{1}{70}-\frac{1}{16}$ gr. (1–4 mg.), is a pale grey amorphous powder, practically insoluble in water, but soluble in rectified spirit and in chloroform. Nitric acid renders it yellow, hydrochloric acid blood-red, and sulphuric acid in excess yellow, fluorescent, and ultimately bright red or violet-red. It is bitter and acrid, causing tingling and numbness, and very irritating to the nostrils, but without odour. Unguentum Veratrinæ (U.S.P.) contains 4 per cent. (B.P. 1898, 2 per cent.) and Oleatum Veratrinæ (U.S.P., B.P.C.) 2 per cent. of veratrine.

Pharmacology.—Its activity is between $\frac{1}{5}$ and $\frac{1}{10}$ of aconitine, and doses of 0·005 gm. ($\frac{1}{13}$ gr.) produce tingling sensations and discomfort, while doses of 0·02 gm. ($\frac{1}{4}$ to $\frac{1}{3}$ gr.) and upwards produce vomiting, purging and great depression. A protoplasmic poison, it kills low forms of life, and this explains why cevadilla has been used to destroy parasites.

Contact Actions.—When it is applied to the skin with friction in a fatty basis it causes tingling, numbness, coldness and sensations of local swelling. When it was applied in a strength of 1 in 10 Cash observed little local anæsthesia, but considerable depression of the thermic sense. When administered hypodermically it causes pain and subsequent numbness. Its action on mucous membranes is very irritating. It causes violent sneezing and discharge of mucus from the nose, and strongly irritates the mucous membrane of mouth, throat, stomach and intestine. The effects produced on the last-mentioned membranes when reinforced by the actions exerted on the muscles of the organs, explain why vomiting and diarrhœa occur more frequently, and to a greater extent, than they do after administration of aconitine.

Absorption.—It is absorbed fairly rapidly and produces very many of the actions described as produced by aconitine, which actions it is, therefore, unnecessary to describe in detail. Thus in the frog a lethal dose causes paralysis of respiration, cardiac infrequency and irregularity, diminution of reflex excitability, together with paralysis of motor conductivity, not only of the cord, but also of the peripheral nerves. There are additional symptoms to be observed, however, gaping movements (usually denoting irritation of the vomiting mechanism, either central or peripheral), fibrillary twitchings of muscles and, in a special degree, a form of incoordination which is sufficiently peculiar to necessitate further description.

A frog poisoned by veratrine springs normally, but lands prone with its legs ex-

tended, and they remain extended for some time before they are drawn up. When the frog is stimulated repeatedly the intervals of prolonged extension become shorter—till the animal jumps quite normally. After a prolonged period of rest the same train of symptoms reappears. The spasm is not caused by slow, crawling, spontaneous movements, nor by the contractions of the respiratory muscles (Cash), and is due to a peculiar poisoning of the skeletal muscles, which is characteristic of veratrine. It is probably not a true tetanic contraction, though it has some features in common with it. In isolated muscles it has been observed that the muscular contraction, following on an induced single stimulation, is stronger than normal, sometimes appearing to consist of more than one simple contraction superimposed. Such a contraction gives a tracing of a higher curve than does an unpoisoned contraction, and the relaxation is so delayed that the tracing of this portion may be thirty times as long as that of normal relaxation. Repeated stimuli cause successive shortening of the height and of the relaxation curves, until a normal curve is obtained. In addition the poisoned muscle responds to weaker stimuli, and can perform more work than the unpoisoned. Veratrine probably increases katabolic changes in the muscle, so that the store of energy is increased during rest, but used up during repeated contractions. If the vitality of the muscle be depressed by fatigue, cold, or by depressing poisons, such as potassium salts, veratrine produces its characteristic effect less strongly, if at all. All muscular tissue is affected by veratrine, skeletal, non-striped and cardiac. The action on plain muscle explains the occurrence of vomiting and diarrhœa with pain, the stomach and intestines being violently contracted and irregularly relaxed as well as irritated, while the secretions are increased. The uterus, bladder, bronchioles, and blood-vessels undergo similar contractions due to peripheral muscular poisoning. The symptoms due to the muscular action in warm-blooded mammals and man appear less prominently in connection with the voluntary and more prominently in the involuntary muscles. Thus abortion, expulsion of urine, and increased blood pressure, as well as vomiting and diarrhœa, have occurred during veratrine poisoning.

On the central nervous system the resemblance of its actions to those of aconitine is remarkably close, and a description of the one serves almost equally well for the other.

On the circulation the muscular action on the ventricle and that on the peripheral circulation introduces additional factors. On the heart the ventricular contraction is increased, and diastolic expansion diminished, an action much more conspicuous in the cold-blooded than on the warm-blooded heart. In the mammal, therefore, the central inhibitory phenomena are the more conspicuous, but the blood pressure is higher, not so much from increased ventricular contraction as from peripheral vascular constriction.

With regard to respiration, temperature, secretions, metabolism and excretion, the similarity between the actions of aconitine and veratrine is sufficiently close to render their recapitulation unnecessary, except to observe that the action is less in amount, but that the constriction of the bronchioles renders the respiratory difficulty more pronounced and sometimes even asthmatic in character.

Therapeutic Uses of Veratrine.—These are entirely confined to the relief of painful conditions, in which cases the ointment is used locally.

Veratrum viride (Green Hellebore) is not official in the B.P. Veratrum (U.S.P.) may be obtained from Veratrum viride or album. Tinctura Veratri (U.S.P., B.P.C.) 5–30 min. (3–20 dl.) is its only preparation. Its composition is very complex, five or six alkaloids having been isolated and investigated. Those which are active have the actions either of aconitine or of veratrine. The combination of these actions appears to cause cardiac weakness and slowing without increased blood-pressure when veratrum is administered in therapeutic doses. The depression of the circulation is intensified by irritation of the alimentary canal, inducing reflex inhibition, which is maintained for a considerable period, accompanied by nausea and, if the dose is sufficiently large, by vomiting. The coincident depression of the circulation, and of the central nervous system caused by it, have led to its use in conditions of convulsions associated with high blood pressure and rapid pulse, in which cases it has been reported to act beneficially, but not so definitely as to render minute examination of all the constituents essential.

Therapeutic Applications of Veratrum Viride.—In puerperal eclampsia the most frequent use of this substance is made and a preparation made for hypodermic administration, and said to contain veratroidine and jervine, has proved efficacious, and can be administered where it is impossible to give the tincture by the mouth (v. ***Ed. Med. Journal***, new series, Vol. XI, p. 313).

Veratrum album (White Hellebore) contains an alkaloid, proto-veratrine, $C_{32}H_{51}NO_{11}$, probably a compound of the base cevine with isobutyric acid. It is nearly as active as aconitine, and acts on muscles by increasing the contractions and power without, however, prolonging relaxation. It does not paralyse motor nerve-endings.

Staphisagriæ Semina (B.P.) are the dried ripe seeds of Delphinium Staphisagria, irregularly triangular, with a soft, oily interior—odourless, but with a bitter, acrid, nauseous taste. They contain an alkaloid, Delphinine, $C_{22}H_{35}NO_6$, with

much the same action as that of aconitine, but less active; another alkaloid which paralyses motor nerve-endings (Staphisagrine), some other unimportant alkaloids and some fixed oil.

The only action made use of is the toxic action on low forms of life, there being an official ointment (about 18 per cent.) used to destroy parasites on the skin. It is not absorbed rapidly, but stimulates and then paralyses sensory nerve-ends. It depresses the motor nerves, and consequently fibrillary muscular contractions are not usually observed. The respiration and circulation are depressed by a large dose, as they are by aconitine, and vomiting and intestinal stimulation are more conspicuous.

Therapeutic Application.—It is used to destroy pediculi.

Preparations of Aconite and Stavesacre

Aconiti Radix. B.P. and U.S.P. Not less than 0·4 per cent. of ether-soluble Alkaloids.
Fluidextractum Aconiti. U.S.P. 0·4 per cent. of Alkaloid. 1 min. (5 cl.).
Tinctura Aconiti. B.P. and U.S.P. (Twice strength of B.P. 1897.) Not less than 0·04 per cent. of ether-soluble Alkaloids. Dose, 2–5 min. (12–30 centimils).
Linimentum Aconiti. B.P. 0·2 per cent. of Alkaloids.

Linimentum Aconiti Compositum (ABC Liniment)	B.P.C.	Lin. Aconiti	2.
		Lin. Belladonnæ	2.
		Chloroformi	1.

Aconitina. B.P. and U.S.P. Dose, $\frac{1}{640}$ gr, (0·1 mil.).
Unguentum Aconitinæ. B.P. 2 per cent.
Chloroformum Aconitinæ. B.P.C. 0·23 per cent.
Veratrina. U.S.P. (N.O., B.P. 1914.) Dose, $\frac{1}{30}$ gr. (2 mg.).

Unguentum Veratrinæ	U.S.P.	4 per cent.
Oleatum Veratrinæ	U.S.P.	2 per cent.

Veratrum Viride

Fluidextractum Veratri	U.S.P.	1–2 min.	6–12 centimils.
Tinctura Veratri	U.S.P.	10–20 min.	6–12 decimils.

Staphisagriæ Semina. B.P. and U.S.P.
Unguentum Staphisagriæ. B.P. 18 per cent. of seeds.

W. C. S.

VASO-CONSTRICTORS AND VASO-DILATORS

The pharmacological properties of the metallic nitrates are totally different from those of the nitrites, for the former are non-poisonous, and their pharmacological action is the same as that of other non-poisonous salts, but the nitrites are highly poisonous and produce a well-marked specific effect upon plain muscle and upon the blood. The organic nitrates resemble the nitrites in their pharmacological properties, and therefore the two groups will be considered together. Amyl nitrite and sodium nitrite are the two most important nitrites in therapeutic use, and nitro-glycerine, erythrol tetra-nitrate, and mannitol hexa-nitrate are all organic nitrates.

Pharmacological Action of Nitrites and Organic Nitrates

Action upon Plain Muscle.—Nitrites produce relaxation of plain muscle both in the intact animal and in isolated organs. The nitrites, therefore, cause vaso-dilatation, dilatation of the bronchi, and relaxation of the gut, ureter, bladder and gall bladder. The action of nitrites in relaxing the arterioles, and thus producing a fall in blood pressure, has been carefully studied, and it is found that the vessels in all parts of the body are relaxed, and that the nitrites produce well-marked vaso-dilatation in regions such as the lungs, in which vasomotor fibres are either absent, or else very feeble, and, therefore, it appears that the nitrites act upon the muscle of the arterioles and not upon the vasomotor nerve-endings. The vaso-dilator action is shown to be peripheral, and not central by the fact that nitrites act as strongly upon the vessels of isolated tissues as upon those of intact animals.

Action upon the Circulation.—Nitrites produce a very well-marked fall in blood pressure, and this appears to be caused entirely by their action upon the vessels, for in moderate doses the nitrites have no action upon the heart. Large doses of nitrites weaken the beat and diminish the output of the isolated mammalian heart.

Action upon the Central Nervous System.—If nitrites are injected into the carotid artery, so that they reach the brain before the peripheral vessels, then they cause a slight initial rise in blood pressure. This rise in blood pressure is caused by the nitrites stimulating the medulla.

Action upon the Blood.—When nitrites are added to blood in a concentration of 1 in 10,000, they reduce the oxyhæmoglobin to methæmoglobin in a few hours, and they produce this action both in vitro and in the intact animal; this reduction of hæmoglobin is not accompanied by any destruction of the red blood corpuscles. Large doses of nitrites will reduce most of the hæmoglobin in the body, and since methæmoglobin is not an oxygen carrier, death ensues from asphyxia.

Excretion.—Amyl nitrite is broken down to form nitrites of the alkalies, and these undergo a partial oxidation and are excreted as nitrates and nitrites in the urine, while a part is oxidised still further and appears as one of the normal nitrogenous excretions. Nitroglycerine and the other organic nitrates are broken down to form a mixture of inorganic nitrates and nitrites. These drugs have no action upon the blood pressure until they are broken down, and the rate at which their action appears depends upon the rate at which they are broken down; for example, Erythrol tetra-nitrate is broken down more slowly than nitroglycerine, and acts more slowly upon the blood pressure.

Therapeutic Action.—Nitrites are used to produce a fall in blood pressure, and also to relieve pain caused by the spasmodic contraction of plain muscle.

The nitrites and the organic nitrites all act in the same manner, but the rate of action varies very greatly with different drugs. Amyl nitrite acts in a few seconds, and its effects last only for a few minutes; it is, therefore, very valuable for rapidly relieving pain in certain cases of angina pectoris, and for relieving bronchial spasm in

asthma, and can also be used in cases of intestinal, renal, or gall stone colic, but amyl nitrite will not produce a long-continued fall in blood pressure. Sodium nitrite and nitroglycerine both produce a fall in blood pressure after a few minutes, and their action lasts about two hours, whilst erythrol tetra-nitrate and mannitol hexa-nitrate only begin to act after about two hours, and their effect upon the blood pressure lasts for several hours.

Nitrites can be administered with advantage in cases of abnormally high blood pressure, and especially in the case of weak hearts struggling against a high aortic resistance, but the beneficial action upon the heart in such cases is due to the lowering of the resistance against which the heart is contracting, and not to any direct effect upon the heart. The administration of nitrites in cases of heart failure under chloroform anæsthesia is wholly irrational, and so also is the exhibition of nitrites in cases of heart disease in which the blood pressure is not raised. Nitrites will relieve headaches due to abnormally high blood pressure, but will only aggravate those due to cerebral anæmia.

Toxic Action of Nitrites.—The nitrites have a powerful pharmacological action, and excessive doses produce methæmoglobinæmia, and this may produce death from asphyxia. This action is of importance because in certain abnormal conditions nitrates may be reduced to nitrites in the alimentary canal, and cases of nitrite poisoning have followed the administration of large doses of bismuth subnitrate. Cows also have been poisoned by eating Chile saltpetre that had been spread upon grass as chemical manure.

The therapeutic action of nitroglycerine depends upon the breakdown of this substance and the consequent formation of nitrites, but nitroglycerine itself produces an action upon the central nervous system, and, when injected into frogs, produces convulsions. Large doses of nitroglycerine in man produce severe headaches, and this effect appears to be due to the drug being absorbed unchanged, and acting upon the brain.

Materia Medica

1. Amyl Nitris (B.P.), Amylis Nitris (U.S.P.). 2–5 min. (12–30 cl.); by inhalation.
2. Spiritus Glycerylis Nitratis (U.S.P.). 1 min. (6 cl.).
3. Liquor Trinitrini (B.P.). ½–2 min. (3–12 cl.).
4. Tabellæ Trinitrini (B.P.). Each contains $\frac{1}{130}$ of a gr. (0·5 mg.) of nitroglycerine.
5. (Liquor Ethyl Nitritis (B.P.). 15–60 min. (1–4 ml.).
6. Sodii Nitris (B.P., U.S.P.). ½–2 gr. (3–12 cg.).
7. (Spiritus Ætheris Nitrosi (B.P., U.S.P.). 15–60 min. (1–4 ml.)
8. Erthyrol Tetra-nitrate (B.P.C.). ½–1 gr. (3–6 cg.).

Non-official.

9. Mannitol Hexa-nitrate. 1 gr.

Barium and Strontium

Pharmacological Action.—Barium acts upon all muscle whether striped, plain or cardiac; in small concentrations it increases the activity of the muscle, and in higher concentrations it produces rigor or systole. In striped muscle it produces a prolonged violent contraction, resembling that produced by veratrine. It causes violent colicky contractions in all plain muscle in the body, and, therefore, when injected into a mammal, it causes violent movements of the gut, uterus and bladder, and also produces an intense vaso-constriction. Barium in small doses causes an increase in the strength of the heart beat, both in the intact animal and in the isolated heart, and in large doses it produces systolic arrest: this action resembles that produced by an excess of calcium, and also shows a superficial resemblance to the action of the cardiac glucosides. The action of barium upon muscle is, in all cases, due to its direct action upon the muscle cells. In large doses barium paralyses the central nervous system.

Barium, strontium and calcium are closely related chemically, and the three elements show a certain gradation of physiological activity in relation to their action upon the frog's muscle and heart. In some respects barium and strontium can partly replace calcium, though to a very limited extent. It is stated that barium can partly replace calcium in the coagulation of the blood. Barium is excreted in the urine and by the bowel.

Therapeutic and other Uses.—Barium is but little used as an internal remedy in therapeutics; it has been recommended in the treatment of various forms of tremor, but there is no evidence that it is of any value in such cases. In veterinary practice barium is sometimes given intravenously as a purge. Barium sulphide is used very extensively as a depilatory, and is the chief constituent of most of the proprietary preparations sold for this purpose. Barium carbonate is used largely as a rat poison. It is of interest to note that the waters of Llangammarch Wells contain three-quarters of a grain of barium chloride in 20 fluid ounces, and are, on this account, recommended in cases of cardiac disease.

Materia Medica

1. Barii Chloridum (B.P.C.). ¼–2 gr. (15–120 mg.).
2. Barii Hypophosphis (B.P.C.). ¼–1 gr. (15–60 mg.).
3. Barii Sulphidum (B.P.C.). ½–1 gr. (3–6 cg.).
4. Strontii Bromidum (B.P., U.S.P.). 5–30 gr. (3–20 dg.).
5. Strontii Iodidum (U.S.P.). 5–15 gr. (3–10 dg.).
6. Strontii Salicylas (U.S.P.). 5–15 gr. (3–10 dg.).

The Mode of Action of Drugs that Produce Vaso-Constriction and Vaso-Dilatation

The drugs that produce vaso-constriction and vaso-dilatation may be divided into—

1. Substances that act upon the central nervous system, or that produce their action by reflexly exciting the vasomotor centres in the medulla.
2. Substances that act peripherally upon nerve-endings, or upon ganglion cells.
3. Substances that act upon the muscles of the arterioles.

These classes will be considered separately.

1. Drugs that Influence the Vasomotor Centres. The vaso-constrictor centre is much more powerful than the vaso-dilator centre : hence any general stimulation, either direct or reflex, of the medullary centres produces vaso-constriction. A vaso-constrictor reflex may be produced by stimulation of any peripheral sensory nerve, for example, by application of cold to the skin, by stimulation of mucous membranes with irritant gases, by blisters, or by cautery. All drugs that produce a general stimulation of the central nervous system also cause vaso-constriction; for example, strychnine, caffeine, cocaine, prussic acid, or atropine. Excessive stimulation of any sensory nerve produces exhaustion of the vaso-constrictor centre, and the initial constriction is followed by vaso-dilatation : surgical shock appears to be due to such an exhaustion of the vasomotor centres.

All drugs that depress the central nervous system also produce a fall in blood pressure : for example, the hypnotics and anæsthetics.

2. Action of Drugs upon the Ganglion Cells and Nerve-Endings.—The vasomotor nerves form part of the sympathetic outflow, but the cranio-sacral autonomic outflow also supplies vasomotor fibres to certain organs : in all cases the vasomotor nerves are ganglionated, and the arterioles are supplied with non-medullated post-ganglionated fibres. If the different organs of the body are examined, in nearly all cases the arterioles can be shown to receive vaso-constrictor fibres from the sympathetic. In most cases these fibres have a powerful action, but, in the case of the vessels of the brain, lungs, heart and liver, the vaso-constrictor fibres are either absent, or else have an extremely feeble action. The existence of vaso-dilator fibres can only be demonstrated with certainty in a few organs : the arterioles of the salivary gland appear to be supplied by vaso-dilator fibres by the chorda tympani, and the external genitals receive similar fibres from the pelvic visceral nerve. Dale recently has shown that after administration of ergotoxine, which paralyses the motor sympathetic nerves, adrenine will produce vaso-dilatation in all those regions of the body where it normally produces vaso-constriction. This fact suggests that the sympathetic nerves contain both vaso-dilator and vaso-constrictor fibres, and that adrenalin normally excites both sets of fibres, but that the vaso-constrictor fibres have a much more powerful action than the vaso-dilators, and that only when the constrictor fibres are paralysed can the action of the dilator fibres be demonstrated. The blood-vessels are normally kept in a state of partial constriction by constant tonic impulses from the vaso-constrictor centre, and hence any drug that paralyses the sympathetic ganglia or endings (*e. g.* nicotine, apocodeine) produces vaso-dilatation, by cutting off these tonic impulses. The action of drugs upon the nerve-endings may be summarised in the following table.

TABLE I.

Nature and Seat of Action of Drug.	*Effect upon Blood-Vessels.*	*Examples of Drugs.*
I. Drugs which stimulate, and then paralyse, the sympathetic ganglia.	Vaso - constriction, followed by vaso-dilatation.	Nicotine. Conine. Lobeline.
II. Drugs which stimulate, and then paralyse the motor sympathetic endings.	Vaso-constriction, followed by vaso-dilatation.	Tyramine. Ergotoxine. (Hypophysine ?)
III. Drugs which paralyse the sympathetic endings.	Vaso-dilatation.	Apocodeine.
IV. Drugs which stimulate all sympathetic endings (motor and inhibitory).	Vaso-constriction, except when the motor sympathetic endings are paralysed by ergotoxine, when vaso - dilatation occurs.	Adrenalin.

3. Drugs that act upon the Muscle of the Arterioles.—The most important of these drugs are (1) drugs that cause constriction, barium, lead, digitalis, and possibly hypophysine; (2) drugs that cause dilatation; nitrites and organic nitrates, and the products of metabolism, especially CO_2 and lactic acid.

Discussion.—The above summary of the action of drugs upon the blood-vessels shows that a general rise in blood pressure can be produced in three distinct ways by these drugs : firstly, by stimulation of the vasomotor centre, secondly, by stimulation of the sympathetic ganglia, or endings, and thirdly, by general stimulation of the muscle of the arterioles. On

the other hand, a general fall in blood pressure can be produced by depression or exhaustion of the vasomotor centres, by paralysis of the sympathetic ganglia, or endings, or by drugs that act directly on the muscle of the arterioles, and cause relaxation.

Moreover, the blood supply of any single region or organ can be increased in the following manner—

1. Excitation of the vaso-dilator nerves to the organ. (This excitation may be direct or reflex.)
2. Inhibition of the central tonic excitation of the vaso-constrictor nerves to the organ.
3. Vaso-constriction in other organs, thus producing a general rise in blood pressure.
4. By the production, through an increase in the metabolism of the organ, of an increased amount of chemical substances which act directly upon the blood-vessels, and produce vaso-dilatation. When an organ enters into activity, any, or all, of these mechanisms may be employed to increase the blood supply of the organ.

The blood supply of an organ is decreased if local vaso-constriction occurs, and the blood pressure remains constant, or if the blood pressure falls and the vessels of the organ do not relax.

The relative quantities of blood going to the different regions and organs of the body are regulated by the above mechanisms.

Therapeutic Action of Drugs that cause Vaso-Constriction and Vaso-Dilatation

Drugs and other therapeutic measures are employed for the following purposes. (1) To increase the blood supply to any particular region. (2) To produce local vaso-constriction. (3) To lower abnormally high blood pressures. (4) To raise abnormally low blood pressures.

1. The blood supply to any region or organ may be augmented by increasing the activity of the organ, when the local blood supply will be increased by any or all of the mechanisms described on p. 688. Counter-irritation also will produce reflexly a local vaso-dilatation, and thus increase the blood flow through the organ. Finally, certain drugs produce vaso-dilatation in some regions but not in others. For example, alcohol causes dilatation of the skin vessels, but does not affect the splanchnic vessels. Caffeine causes a local dilatation of the kidney vessels, but this may be a secondary effect due to the drug causing an increase in the activity of the kidney. Yohimbine appears to act in a specific manner upon the vaso-dilator centre of the pelvic visceral nerve, and produces vaso-dilatation in the external genitals.

Bier's method of venous congestion is another means of modifying the local conditions of the blood supply: this causes a diminution in the amount of blood passing through the organ, but greatly increases the amount of the lymph flow, and in this latter respect the effect resembles that produced by local vaso-dilatation.

2. The blood supply of an organ is decreased by producing local vaso-constriction. Adrenalin (1 in 50,000) when injected hypodermically stimulates the motor nerve-endings of the sympathetic, and thus produces a local vaso-constriction. Adrenalin is employed in this manner to prevent the diffusion and absorption of local anæsthetics, when these are injected hypodermically, and also to check hæmorrhage in operations on the nose and elsewhere.

3. Drugs used to lower abnormally high blood pressures. The nitrites and the organic nitrates are the chief drugs used for this purpose. These drugs act upon the muscle of the arterioles and thus produce a general vaso-dilatation in all parts of the body.

The blood pressure may also be reduced by diminishing the total amount of fluid in the vessels. This can be done most rapidly and effectively by bleeding, and more slowly by purgation and emesis. This last method was frequently applied in the early part of last century, antimony being regularly administered for this purpose.

4. Drugs used to raise abnormally low blood pressures. An abnormally low blood pressure may be due, primarily, either to failure of the heart, or to failure of the vasomotor mechanism: in practice both factors are nearly always present, but only those cases will be considered here in which the fall of blood pressure is due chiefly to a failure of the vasomotor system. In such cases the heart is not exhausted, but there is an insufficient return of venous blood to the heart, and, in consequence, the heart beats rapidly, but inefficiently.

This condition appears usually to be present in cases of surgical shock, and the essential point in the treatment is to aid the return of blood to the heart. The blood collects chiefly in the veins of the splanchnic region, and, therefore, much may be done by raising the foot of the bed, and by applying pressure to the abdomen. The volume of fluid in circulation also can be increased by saline injections. Drugs, therefore, only form a small part in the treatment of surgical shock. Since insufficient blood is returned to the heart, it is obvious that stimulation of the heart itself by drugs will be of little use: moreover, in severe shock, the vasomotor centres of the medulla are completely exhausted, and therefore medullary stimulants such as strychnine, which normally raise the blood pressure by producing a general vaso-constriction, produce but little effect in shock.

The only drugs likely to be of use in severe cases of shock are those that produce a general vaso-constriction by acting peripherally, either

upon the sympathetic nerve-endings or upon the muscle; such drugs are hypophysine or pituitary extract (seat of action uncertain), and adrenalin and tyramine, which act upon the nerve-endings. The pharmacological action of hypophysine is not yet completely worked out, but the drug appears to have a double action, and may cause vaso-dilatation as well as vaso-constriction. It also causes a general constriction of all the plain muscle in the body, and an especially well-marked constriction of the bronchial muscles and uterus. When the drug is injected intravenously, it causes an initial fall in blood pressure, and then a rise in blood pressure, which may last for twenty minutes: but a second dose of the drug produces only a fall in blood pressure. The drug, therefore, does not appear to be wholly satisfactory for use in the treatment of shock.

Adrenalin produces a strong immediate vaso-constriction, and at the same time increases the frequency and strength of the beat of the heart, but unfortunately its effects are very transitory, only lasting a few minutes. An improved circulation for even as short a time as this, however, may benefit the patient, because the improved blood flow will wash away the poisonous products of metabolism that collect in the tissues, when the blood supply is insufficient.

Tyramine acts in a similar manner to adrenalin, but more slowly, and its effects when given subcutaneously will last for twenty minutes, but, if the dose is repeated, the second injection produces a much feebler action than the first.

There is, therefore, no drug that can be considered entirely satisfactory in the treatment of severe shock, but adrenalin and tyramine appear the most likely to yield beneficial results.

A. J. C.

ERGOT, ECBOLICS AND EMMENAGOGUES

Ergot

Ergot is the sclerotium or compact mycelium of a fungus, Claviceps Purpurea, which commonly infects rye. The long, blackish-purple bodies, bearing an enlarged and distorted resemblance to the grains whose substance the mycelium replaces, were formerly thought to be an abnormal form of the rye-grain, whence the names "spurred" or "horned" rye (Secale Cornutum). The same, or a closely related fungus infects other cereals, though less frequently, and some wild grasses are said to be regularly and heavily ergotised—*e. g.* the tall fescue grass (Festuca Arundinacea) growing over vast, swampy areas in New Zealand.

The consumption of bread or meal containing a considerable proportion of ergot, has given rise to widespread and serious epidemics of poisoning. Two types of ergotism are recognised, one characterised by gangrene, chiefly of the extremities, the other by nervous symptoms—formication, muscular spasms, and convulsions, frequently followed, in non-fatal cases, by impaired intelligence and permanent contractures of the limbs. The gangrenous type has been characteristic of the epidemics in France and South Western Europe, the convulsive type of those in Germany and the northern and eastern parts of the Continent. Suspicious cases affecting isolated families have been recorded in Britain, but no epidemics. The gangrenous type was formerly attributed to "sphacelinic acid" or "sphacelotoxin," the convulsive to an alkaloid "cornutin." It may be regarded as proven, however, that these principles were not chemical entities, but owed their activity to the alkaloid ergotoxine, present in all to a greater or less extent. The gangrenous ergotism can be clearly related to ergotoxine. The ætiology of the convulsive type is more obscure. Possibly ergotoxine can produce these effects also in man, when given in massive doses, so as to produce acute, rather than chronic, effects, and when the resistance of the subject is weakened by the poverty and hardship which have always prevailed in districts where such epidemics have arisen. We shall see that certain putrefactive amines regularly contribute to the activity of ergot, and it is not impossible that abnormal putrefactive products, occurring under certain conditions of weather, or defective storage of the grain, may play a part in the production of these symptoms; but there is no positive evidence in favour of this supposition.

Active Principles.—As long ago as 1875, Tanret described an alkaloid in ergot as existing in two physical states, crystalline and amorphous, and gave to both forms the name "ergotinine." His identification of the two diverted attention for many years from the importance of his discovery, for the crystalline ergotinine, naturally chosen for experiment as more readily purified, was found to be inactive, and active principles were sought in other directions. It is only in recent years that the investigations of Barger and Carr, and of Kraft, have made it clear that the amorphous alkaloid is a distinct substance, being a hydrate of the crystalline ergotinine, and obtainable in pure form by making use of the fact that its salts crystallise. This amorphous alkaloid, for which Barger and Carr's name "ergotoxine" is now commonly used (Kraft proposed to call it "hydroergotinine"), has been shown to be a highly active substance, possessing, among other characteristic actions, the property of producing gangrene. More recently it has been shown that ergot contains the amines derived from amino-acids by splitting off carbon dioxide. These are formed in the putrefaction of proteins by certain bacteria, and the metabolism of the

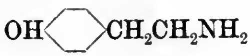
ergot fungus would appear to resemble that of such lower organisms in this direction. Certain of these, in particular p-hydroxyphenylethylamine (from tyrosine) and β-iminazolylethylamine (from histidine), have a powerful physiological action, and they exist in ergot in sufficient proportion to make an important contribution to its physiological and therapeutic activity. It is of interest to note that Buchheim, in 1874, suggested that the activity of ergot was due to no specific principle, but to "putrid and septic substances in general."

The following are the formulæ of the substances mentioned—

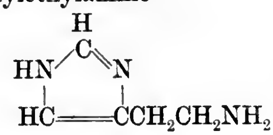
Crystalline ergotinine (Tanret)—$C_{35}H_{39}N_5O_5$.

Ergotoxine (Barger and Carr), or hydroergotinine (Kraft)—$C_{35}H_{41}N_5O_6$.

p-hydroxyphenylethylamine—



β-iminazolylethylamine—



It has recently been shown (Ewins) that certain specimens of ergot contain recognisable amounts of acetyl-choline, another intensely active substance. This, however, is not likely to prove therapeutically important.

Action of the Different Principles

1. **Ergotoxine.**—On the frog ergotoxine has a slight and not characteristic action. The movements become rather sluggish, and the animal is readily fatigued. The action appears to be of the curare type, and in this mild degree is exhibited by many alkaloids.

In the domestic fowl ergotoxine, when injected hypodermically, or intravenously, produces the effects which have long been recognised as characteristic of ergot-poisoning in this species—ataxia, prostration, diarrhœa, dyspnœa, salivation, and pallor and discoloration (cyanosis) of the comb. When ergotoxine is injected intravenously the effect, if not fatal, usually passes off completely in about twelve hours. When it is given hypodermically, so as to secure slower absorption and produce a prolonged, non-fatal, intoxication, the stasis of circulation in the comb generally leads to dry gangrene of the digitations, and a large part of the comb may dry up and be subsequently shed without hæmorrhage. The effects in this species closely resemble those described by Kobert with "sphacelinic acid," and by Jacobj with "sphacelotoxin."

In rodents ergotoxine produces symptoms of varying severity. The chief features of the action are muscular tremors and weakness, dyspnœa and salivation. As little as 3 mg. may be fatal to a medium-sized rabbit when given intravenously, but as much as 10 mg. may be given in the same way to another without fatal result. After a fatal dose, the internal temperature rises rapidly towards, and even after death, temperatures as high as 45° C. being registered in some cases.

In the cat the symptoms following hypodermic or intramuscular injection are more characteristic—vomiting, defæcation, ataxia, salivation and excitement, followed by deep narcosis, in which the pupils are narrowed to mere slits, and do not dilate in the dark. The anal sphincter becomes incompetent and fæces are expressed by light manipulation of the abdomen. In the pregnant female powerful contractions of the uterus can be felt through the abdominal wall and bloody fluid trickles from the vagina. The embryos become asphyxiated and, if the mother survives, are born when the acute symptoms pass off, or may be retained for days. In the cat, again, the fatal dose varies within wide limits; as little as 3 mg. has been known to kill a large cat, while as much as 20 mg. may be tolerated with only brief symptoms by a small one.

The most characteristic effects of ergotoxine, however, only become evident when records are taken of the activity of involuntary muscle in the different systems and organs, in an animal under anæsthetics, or, better, with the brain destroyed. The action is best seen in the cat or dog. Injection of one or two milligrammes causes, in the cat, a prolonged rise of blood pressure, which is entirely due to peripherally excited constriction of the plain muscle of the arterioles. At the same time the uterine muscle acquires an intense tonus, and the pupil is narrowed to a slit. These effects are uninfluenced by section of post-ganglionic fibres, or by atropine. The bladder and intestines are affected in like manner, though in less degree, and the diminution of the artificial respiratory excursions, with steady stroke of the pump, indicates constriction of the bronchioles. Ergotoxine, then, causes general rise of tonus in plain muscle, most marked in the case of the arterioles and the uterus. When the dose of ergotoxine is sufficient, this stimulant action is accompanied and followed by a curious change of response of plain muscle and gland cells, to stimulation of nerves of the true sympathetic system and to adrenalin. This change has the effect of a paralysis of all the sympathetic nerve-endings which are motor or augmentor in function, while those connected with inhibitor action are unaffected. This selective paralysis is seen also in the case of structures, such as the

internal anal sphincter, on which ergotoxine has no primary stimulating action. In the case of some organs, to which the sympathetic system presumably sends only augmentor fibres, ergotoxine simply obliterates the effect of sympathetic nerves or of adrenalin. Thus, after sufficient ergotoxine, neither stimulation of the cervical sympathetic nerve, nor injection of adrenalin, causes any dilatation of the pupil or any secretion of saliva, and the effect of the accelerator nerves and of adrenalin on the heart is reduced almost to vanishing-point. On the other hand, the cerebral and sacral autonomic nerves retain their function unimpaired, so that stimulation of the chorda tympani causes salivary secretion; of the vagus, cardiac inhibition; of the pelvic nerve, contraction of the bladder and rectum, as well after full doses of ergotoxine as before. When sympathetic nerves or adrenalin normally produce inhibitor effects, as on the muscle of the intestinal wall, or the uterus of the virgin cat, these effects are also unaltered by ergotoxine. The most characteristic change is seen in the case of those organs in which a predominantly motor-sympathetic nerve-supply contains an inhibitor admixture. In these the normal motor effect of sympathetic nerves and adrenalin is reversed, *i. e.* changed to inhibition, by ergotoxine. Thus, when ergotoxine has been given, stimulation of the sympathetic nerve-supply, or injection of adrenalin, causes dilatation of the arterioles in carnivora, so that a fall of blood pressure replaces the normal rise; inhibition of the pregnant uterus and the internal anal sphincter in the cat, and of the uterus and bladder in the ferret, in place of the contraction which such stimuli normally produce in all these organs.

In rodents the stimulating action of ergotoxine on plain muscle is less marked. The uterus of the pregnant rabbit is thrown into strong contraction, but no rise of blood pressure is produced in this species. Motor-sympathetic effects, however, are paralysed as in carnivora. In the monkey the only marked stimulant effect of ergotoxine on plain muscle appears to be that on the uterus; but motor-sympathetic effects are paralysed by large doses in this species, as also in other mammalia (pig, goat). A powerful vaso-constrictor effect, causing a large rise of blood pressure, but not followed by sympathetic paralysis, has been observed in the fowl, and may possibly explain the readiness with which gangrene is produced in this species.

In the human subject ergotoxine has been observed clinically to stimulate uterine contraction, but no effect on arterial, or other plain muscle, has been recorded. No human cases of poisoning by pure ergotoxine are on record, but the symptoms of poisoning by ergot, when taken to produce abortion, are mostly similar to those produced by ergotoxine in animals. The peripheral gangrene, characteristic of some of the epidemics caused by ergotised grain, may be attributed, with some confidence, to chronic ergotoxine poisoning.

2. **p-Hydroxyphenylethylamine.**—This base, which has also been found in putrefying protein, autolysed pancreas, cheese, etc., is found in varying proportion in ergot itself, and in fairly large proportion in some watery extracts of the drug, being doubtless formed by ferment action or incipient putrefaction during the extraction process. Its action is similar to, though much weaker than, that of adrenalin (*q.v.*), the latter being roughly fifty times as active on the blood pressure of the cat. Its action is of the "sympathomimetic" type on all the organs on which it has been observed; but whereas adrenalin seems to stimulate inhibitor sympathetic nerve-endings even more powerfully than those of motor function, the reverse is true of p-hydroxyphenylethylamine.

In virtue of its action on sympathetic nerve-endings it causes a large rise of blood pressure, due to arterial constriction and cardio-acceleration, and contraction of the uterus in those species, including the human, in which the muscle of that organ receives a motor nerve supply from the sympathetic system. It is without doubt the substance mainly responsible for the rise of blood pressure, which many specimens of the Extractum Ergotæ Liquidum produce when injected intravenously, and which has been suggested as an index of their therapeutic activity. There are other pressor bases, belonging to the same series of amines, derived from amino-acids (isoamylamine, indol-ethylamine), and these almost certainly occur in ergot, but not in such proportion as to contribute in any significant degree to its activity.

3. **β-Iminazolylethylamine.**—This base bears the same relation to histidine as p-hydroxyphenylethylamine does to tyrosine, and is similarly produced by putrefaction, as well as by the ferments of ergot and other fungi. It is the most intensely active of the ergot principles, but usually occurs in ergot in small proportion. Some extracts made by dialysis, during which ferment action and putrefaction may go on for a long time, contain it in relatively high proportion, and exhibit its action with great intensity.

The characteristic action is an intense stimulation of plain muscle. This is most conspicuous in the case of the uterus, but is well marked in the case of other organs, such as the alimentary canal. It causes constriction of the arteries when perfused through isolated organs, and this vaso-constrictor action is reproduced in some species (rodents) when the base is injected intravenously into the animal,

a rise of blood pressure being the result. In other species (carnivora, monkey) it causes, when so injected, a vaso-dilator fall of systemic blood pressure, the mechanism of the action being, in this case, inadequately explained as yet. In sufficient doses (1 mg. or more) it produces intense spasm of the muscular coats of the bronchioles, and in highly susceptible animals, such as the guinea-pig, even minute doses may produce this effect with such intensity as to cause death by asphyxia. The action of β-Iminazolylethylamine has an interesting similarity to that of the "depressor substance" which occurs in decoctions of many animal organs, and the symptoms which it produces are in most respects identical with those which constitute the "anaphylactic shock." Agmatine, the analogous amine from arginine, has been stated to have an action of the same kind, but this is, in any case, very weak.

Therapeutics.—The only really important use of ergot is to stimulate contraction of the uterine muscle, though it has been administered in various forms of hæmorrhage, such use being probably based on a false analogy from its undoubted value in checking uterine hæmorrhage. It is also reputed to be of value in enuresis and chorea, though there is no rational basis for such an action. Sufficient clinical data are not yet available to warrant any very definite statement as to the therapeutic value of the active principles used separately, and in pure form. Such evidence as there is points to the probability that the simultaneous use of all, as in ergot administration, will give better results than that of any one of them alone. But even in regard to the use of ergot itself clinical evidence has no real unanimity. The early discussions, as to whether the drug had any value, may be regarded as long ago settled in its favour; but the propriety of its use, before the third stage of labour is complete, is still a matter of debate. The divergence of medical teaching on this point is probably attributable in part to a difference of dosage. There is, at least, no pharmacological inconsistency in the view that the drug may be used in large doses to cause tonic contraction of the uterus, when labour is complete, while small doses will increase the excitability of the uterine muscle to normal stimuli in the earlier stages, without necessarily introducing risk of the dreaded "tetanus uteri." But the drug itself, and still more its preparations, contain the different active constituents in such variable proportions, that it is easy to understand that one observer may see only favourable results, even when using apparently the same dosage as, in other hands, has led to disaster. It is clearly, therefore, of primary importance that some method of checking the activity of the drug should be available, and that the methods laid down for the preparation of extracts and tinctures should be such as will ensure the presence of all the natural active constituents, and avoid extraneous addition to them during the extraction process.

Standardisation and Preparations.—An ideal assay of ergot should indicate the proportions of ergotoxine, and of both the important amines present in the sample. In the case of the drug itself only the ergotoxine estimation seems practicable; and this is probably sufficient, since ergotoxine is the most unstable constituent. Its presence in adequate proportion is a guarantee of the soundness of the specimen, and the indications are that, in ergots with good ergotoxine content, the proportions of the amines do not vary widely. Probably a satisfactory chemical method for the estimation of ergotoxine will be devised eventually; meanwhile estimates of the ether-soluble alkaloid, including both ergotinine and ergotoxine, such as that devised by Keller, give an approximate indication. Two of the various proposed physiological methods of assay—the estimation of the dose necessary to produce a definite cyanosis of the cock's comb, and that of the dose producing the "vasomotor reversal" in cats—are essentially ergotoxine estimations, and therefore suitable for application to the testing of the drug itself, as suggested above. It is doubtful whether either is more accurate, even than the crude chemical method already available. Attempts to apply them to preparations containing practically no ergotoxine, owing to the mistake of regarding "ergot" as a pharmacological unit, have naturally failed.

Turning to the preparations, the only official extract which at all fulfils the demand that it shall present all the activity present in the ergot, and that only, is the fluid extract made with moderately dilute alcohol, acidulated with a weak acid (acetic), which extracts and keeps in solution the ergotoxine as well as the amines present in the ergot.

The process for the Extractum Ergotæ (Ergotin) begins well by extracting with 60 per cent. alcohol, which extracts the ergotoxine. But when hydrochloric acid is added to the concentrated extract at a subsequent stage, the ergotoxine is practically all carried down with the resinous precipitate which is then formed, and which is filtered off and discarded. The Extractum Ergotæ Liquidum, being a watery extract, contains only variable traces of ergotoxine, but is rich in the amines. The double and prolonged maceration with water gives ample scope for continued action of ferments and for putrefaction, so that

the final extract is often disproportionately rich in the amines, and probably in other products of incipient putrefaction. It is the most widely used in England of any of the ergot extracts, and there is no reason to doubt that it has some therapeutic activity, chiefly due to the amines; but it cannot be considered as representative of ergot. The ammoniated tincture is probably a good preparation when quite freshly made, but the presence of the ammonia, which sets the ergotoxine free as a base, cannot be conducive to stability. If an alcoholic preparation, more dilute than the fluid extract, is required, it should, like the latter, be made with alcohol acidulated with a weak organic acid.

Preparations

Ergota (B.P., U.S.P.). Ergot of rye.
Dose : (in powder) 15–60 gr. (1–4 g.).
Extractum Ergotæ (B.P.). Ergotin.
Dose : 2–8 gr. (12–50 cg.).
Extractum Ergotæ (U.S.P.).
Average dose : 4 gr. (2·5 dg.).
Extractum Ergotæ Liquidum (B.P.).
Dose : 10–30 min. (6–18 dl.).
Fluidextractum Ergotæ (U.S.P.).
Average dose : 30 min. (2 ml.).
Infusum Ergotæ (B.P.).
Dose : 1–2 fl. oz. (30–60 ml.).
Injectio Ergotæ Hypodermica (B.P.). A solution of ergotin in water with a little phenol.
Dose : 5–10 min. (3–6 dl.).
Tinctura Ergotæ Ammoniata (B.P.).
Dose : $\frac{1}{2}$–1 fl. dr. (2–4 ml.).
Vinum Ergotæ (U.S.P.). Fluid Extract diluted with white wine and alcohol.
Average dose : 2 fl. dr. (8 ml.).

Ecbolics and Emmenagogues

The substances, which have a reputation as ecbolics or emmenagogues, form an ill-defined class, and those which are of value are, for the most part, dealt with under other headings, since their action on the uterine function is incidental to, or forms merely one aspect of an action of more general type.

Thus an amenorrhœa secondary to chlorosis is benefited by iron, while aloes assists in restoring a suppressed menstrual flow by producing congestion of the pelvic viscera. The action of ergot and of pituitary extract is dealt with elsewhere. It is hardly too much to say that there is no substance having a reputation for ecbolic or emmenagogue action alone, which has any legitimate place in therapeutics. The interest of these drugs is rather medico-legal.

Of the many substances enjoying a concealed popularity, fostered by quacks, for their supposed efficacy in terminating pregnancy in its early stages, most are without effect, and those which produce abortion only do so in doses sufficient to kill a large proportion of patients. Lead probably acts by intense stimulation of the uterine muscle, causing asphyxiation and death of the fœtus. Ergot, when it produces abortion, probably does so by a similar action. Of the others, it is of interest to note that several produce fatty degeneration of the liver—phosphorus, oleum pulegii (oil of pennyroyal), myristica (nutmeg). These produce abortion when they kill the fœtus before the mother. They have no direct action on the uterus.

When it is necessary to empty the uterus or to induce premature labour, ergot and hypophyseal extract have valuable adjuvant action to operative procedure, but neither is certainly or even commonly effective by itself. Certain of the essential oils, apart from their poisonous action in large doses, probably have, in small doses, a reflex effect on the uterus through their mild, stimulating action on the gastric mucous membrane, and on the urinary tract during their excretion, and may thus assist in relieving pain in dysmenorrhœa, and in increasing a too scanty menstrual flow. As a class, however, the "ecbolics and emmenagogues" were better removed from pharmacology. H. H. D.

THE CINCHONA ALKALOIDS

1. **Source.**—These substances are derived from plants of the natural order Rubiaceæ (the madder tribe) and of the genera Cinchona and Remijia. They were originally indigenous on the eastern slopes of the Andes, but since the middle of the last century have been cultivated in India, Ceylon and Java. About 80 per cent. of the bark imported into the United Kingdom is brought from the last-named island.

About thirty-six species are known to yield the cinchona alkaloids, but only a few of these in sufficient quantity to be available for commercial purposes. In this country C. succirubra alone is recognised for preparations of cinchona, which must contain 5 to 6 per cent. alkaloids, one half as quinine and cinchonine. In the United States C. Ledgeriana, C. Calisaya, C. officinalis or hybrids of these, and also red cinchona bark, derived from C. succirubra are recognised. The latter must contain 5 per cent. total alkaloids, the former group 5 per cent. total alkaloids, 4 per cent. of which must be ether soluble.

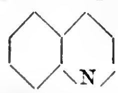
The various alkaloids may be prepared from any species, and, in fact, hybrids or grafts of C. Ledgeriana on the more hardy sorts, such as succirubra, are the source of a great part of the bark now imported.

2. **History.**—Cinchona was introduced into Europe shortly after the conquest of South America by the Spaniards, in the third decade of the seventeenth century. The name is said

to be derived from the Countess of Cinchon, wife of a Spanish viceroy, who was treated for malaria by preparations from the bark. There is little evidence that cinchona was used by the Peruvian natives. It gained acceptance as a remedy for ague or malaria fairly rapidly in Europe, and appeared in the London Pharmacopœia of 1677 as Cortex Peruanus. Some of the chemical constituents were separated in a more or less impure state towards the end of the eighteenth century; quinine and cinchonine were obtained by Pelletier and Caventon in 1820, and the composition of the former accurately determined by Liebig, Regnault and Strecker.

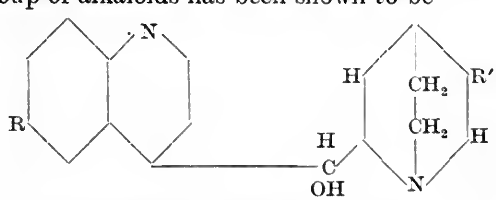
3. **Chemical Composition.**—About thirty alkaloids have been separated from Cinchona and Remijia bark, and the chemical composition of all but a few of these has been determined. Only five, however, are of any importance medically, namely, quinine, quinidine, cinchonine, cinchonidine and cupreine. They occur combined with cinchotannic, quinic and other acids. The former yields a red colouring matter on oxidation, called cinchona red.

Quinine and quinidine are isomeric substances which rotate polarised light in opposite directions, and are probably stereo-isomers. Their empirical formula is $C_{20}H_{24}O_2N_2$, and structurally they consist of a double ring, one ring being a derivative of quinoline



and the other a heterocyclic ring, also containing nitrogen.

Cinchonine and cinchonidine represent a similar stereo-isomeric pair, and contain the same double ring. The general formula for this group of alkaloids has been shown to be—



In quinine and quinidine

$$R = OCH_3,\ R' = CH:CH_2$$

In cinchonine and cinchonidine

$$R = H,\ R' = CH:CH_2$$

In cupreine

$$R = OH,\ R' = CH:CH_2.$$

The chemical difference between these bodies can therefore be expressed as follows—

Quinine and quinidine	$C_{19}H_{21}ON_2.OCH_3$
Cinchonine and cinchonidine .	$C_{19}H_{21}ON_2.H$
Cupreine	$C_{19}H_{21}ON_2.OH$

All these bodies are diacidic bases, yielding two series of salts, acid and neutral. Many of these salts are used in medicine, their important differences being: (1) the amount of the base which they contain, and (2) their solubility in water.[1]

4. **Pharmacology.** *Cinchona.*—The pharmacological properties of all the cinchona alkaloids are very similar, the action of preparations of the bark itself depending on the constituent most largely represented. C. ledgeriana usually contains a high proportion of quinine, C. succirubra a larger amount of cinchonine and cinchonidine. At the present time, however, these differences are of little practical importance, as the infusion and tincture are only used as "bitters," and might be deleted from the Pharmacopœia without much loss. The old "tonic" of bark and steel wine is chiefly remarkable for its nastiness. We can, therefore, proceed at once to consider the action of the alkaloids themselves, beginning with the most important of them, namely, quinine.

Quinine and its Salts.—The action of quinine is general in character, and depends on its property of depressing protoplasmic activity after a transitory period of exaltation, which is noticeable only when small doses or dilute solutions are used. This has been abundantly shown in experiments on simple animal and vegetable cells of many kinds, the only important exception being certain moulds and bacteria which are very resistant to the action of the drug. Most of the effects of quinine when absorbed into the bodies of animals or man can be traced to this general action on protoplasm, very little selective action on any particular cells or organs being seen. Besides its action on living cells quinine also retards the action of certain ferments, notably the oxidases.

When taken into the stomach it has the usual action of bitter substances; in small doses it increases the appetite and acts as a stomachic, in larger doses it is irritant and produces pain and vomiting. Some absorption occurs in the stomach, but the greater part is absorbed in the duodenum; the completeness and rapidity of absorption depending on the solubility of the salt used and the integrity of the walls of the alimentary tract. In diseased conditions of the bowel and liver, absorption is not so complete.

Quinine is usually somewhat rapidly and completely eliminated by the kidneys, but individual variations occur. It is generally supposed that most of the alkaloid passes out of the body unchanged, but a proportion is apparently oxidised. The exact amount has

[1] A full account of the chemistry of the cinchona alkaloids will be found in Dr. T. A. Henry's work, *The Plant Alkaloids* (1913), to which the writer is indebted for many of the newer facts in this article.

been variously stated as 10 per cent. and 40 per cent. The chemical changes occurring in the altered portion are also somewhat uncertain, but it appears that in any case they result in the production of a physiologically inert substance.

It is probable that the concentration of the alkaloid in the blood serum never reaches 1 per cent., which is the minimum necessary to damage the cells of the normal kidney.

Quinine has little effect on the central nervous system, heart or respiration, but large doses produce a short period of excitation followed by depression. Quinine may, perhaps, in large doses, cause convulsions, and some other cinchona alkaloids certainly have this effect. In the rare cases of poisoning in man and in experimental poisoning in animals, there is progressive collapse, with failure of respiration, and subsequently of cardiac action. In smaller doses, especially in susceptible persons, a series of symptoms termed "cinchonism" is observed. The most prominent is deafness, buzzing and humming noises in the ears, and, in very rare cases, permanent loss of hearing. The fields of vision, especially for colours, may be contracted, and, again very rarely, total blindness may occur. Transient rashes are sometimes noticed.

The action of quinine on unstriped muscle is, again, one of short excitation followed by relaxation. Thus the arterioles are contracted and then dilated, and with large doses the uterus may be stimulated to contract, but this effect is very inconstant.

The most important action of quinine on the organism is its effect on metabolism, and though this subject has not yet been quite satisfactorily elucidated, the following summary may be taken to represent the views most generally accepted.

Owing to its action as a protoplasmic poison, quinine retards metabolism; but this only applies to nitrogenous metabolism, the total nitrogen excretion falling, but the absorption of oxygen and the excretion of carbon dioxide are unaffected. The decreased excretion of nitrogen is taken to mean the storage of nitrogenous substances in the body, possibly in the form of substances intermediate between the ingested proteins and the final product urea, with a consequent saving of heat production. The drug is also supposed to have some slight action on the heat-regulating centres, whereby the diminished heat production is not compensated by diminished heat loss. In some cases possibly there may be, in addition, an increased heat loss from the skin. Thus quinine acts as an antipyretic, but mainly owing to its inhibitory power on heat production.

Quinine has also a certain action on the blood; small repeated doses are said to increase the number of red blood cells and the amount of hæmoglobin; the leucocytes, especially the polymorphonuclears, are also increased (de Sandro). In larger doses a reverse effect is produced, and in experiments on the web of the frog's foot the leucocytes have been seen to assume a globular shape and to cease to respond to mechanical injuries by diapedesis.

Thus quinine is said to check suppuration, but it must be evident that this is not a therapeutic action, as it merely means that one of the defensive forces of the body is paralysed.

It has already been mentioned that quinine acts on the special senses; probably this is a peripheral effect, and there seems no reason to doubt that when applied locally it has an inhibitory action on the terminations of the sensory nerves in skin and muscle.

The Remaining Cinchona Alkaloids.—These are of little importance therapeutically, as their action in general resembles that of quinine, *i. e.* they are all protoplasmic poisons. The four chief alkaloids have been contrasted as regards their several actions by various observers; as antiseptics they have been placed as follows: quinine (most active), quinidine, cinchonidine, cinchonine. As muscle poisons, cinchonidine (most active), quinine, cinchonine, quinidine. As heart poisons, cinchonidine (most active), quinine, cinchonine, quinidine.

Cinchonidine, however, differs in degree from the others in being a convulsant poison. Rather large doses produce epileptiform fits; cinchonine acts similarly, but not so powerfully.

None of the other alkaloids have been shown to be superior to quinine in their action on the malarial parasite, and most of them are known to be inferior.

5. **Therapeutics.**—The *general indications* for quinine and its salts may be easily deduced from a consideration of its pharmacological action. In small doses it acts as a bitter stomachic, improving digestion and appetite, and possibly the condition of the blood. In larger doses it acts as an antipyretic by inhibiting nitrogenous metabolism and diminishing heat production, both of which are increased in febrile conditions. It cannot be said to be of much value in increasing uterine contractions, as large doses are required and the effect is very uncertain.

Externally quinine may be used as an antiseptic, but is too expensive for ordinary purposes. Solutions of the strength of 0·5 per cent. have been employed in various affections of the eye (conjunctivitis, etc.) and as injections in gonorrhœa. It is also a frequent ingredient in hair lotions.

The Oleatum is intended for absorption by the skin, but the value of this method of administration in malaria is doubtful. Eight grains to one ounce of cod-liver oil has been recommended as an application to the skin

previous to treatment by the X-rays. A dusting powder of quinine has been employed as an anæsthetic and caustic antiseptic in syphilitic chancres (Sylvestrini).

Internally quinine has been thought to be of value in many acute infections, but it is more than doubtful whether it has any direct bactericidal effect. Its action as a protoplasmic poison seems to be less marked on less differentiated and more vegetative cells, such as bacteria, than it is on such higher and more definitely animal organisms as the protozoa. Still quinine is often given in *pneumonia*, in fairly large doses, and though it does not apparently abort or shorten the attack, it seems to exert a beneficial effect on the patient in some cases, and to ease the respiration. In *influenza* it is a rather favourite remedy, and it enjoys the confidence of the public, if not of the profession, as a prophylactic against the "common cold."

Quinine has also been given in various neuralgic affections, but it is doubtful if it has much effect, unless they are definitely malarial in origin.

In *whooping cough* quinine has long been given, apparently with a view of destroying the causal organism, having been advocated by Binz in 1868. One and a half to three grains of the hydrochloride has been recommended, three or four times daily, in water. Binz himself gives as many decigrams each day as the child's age in years, and under one year as many centigrams as the child's age in months. The daily dose, therefore, will be progressively $\frac{1}{6}$ to 2 gr. during the first twelve months (1–12 cg.), 3 gr. at two years, $4\frac{1}{2}$ at three years, $6\frac{1}{4}$ at four years, $7\frac{3}{4}$ at five years, and so on, up to $15\frac{1}{2}$ gr. at ten years. The bitter taste may be minimised by prescribing the tannate or one of the insoluble quinine compounds (*vide infra*).

As an *antipyretic* in any febrile condition quinine has probably been somewhat unduly neglected of late years, owing to the introduction of the aniline derivatives. It has the advantage over these, however, in not depressing the respiratory and circulatory systems to any marked extent, and, at any rate in bronchitis and the milder febrile conditions where an antipyretic may be of use, it is probably the best. It must, however, be given in fairly full doses, which are not tolerated by all individuals.

We may now consider the special object for which quinine is most largely employed, namely, to arrest or cure **malarial fever.** This action of the drug does not depend upon its effect on the host, but upon its effect on the parasite, which is almost specific.

Quinine or its salts are given in malarial countries for two purposes, namely, as a prophylactic and as a curative agent. Quinine, when absorbed into the body, circulates in the blood stream for a certain period—one-half is said to be excreted in six hours and the remainder passes out gradually during the next few days. As very dilute solutions *in vitro* inhibit the movements of the Plasmodium malariæ, it is sufficient to keep small amounts of the drug constantly circulating in the blood in order to obtain a fair amount of protection. Usually 5 to 15 gr. (0·3–1·0 gm.) is given daily, but old residents in malarial districts frequently take an indeterminate dose, much as people in colder climates suck formamint lozenges to avert a sore throat. When given as a remedy, however, much depends on the details of administration. The object is, in the first place, to attack the parasite when in its least resistant stage, namely, just when sporulation occurs and the enhæmospores are set free in the blood. For this purpose a large dose should be given (10–15 gr. or 0·8–1·0 gm.) three times daily, for two or three days before the onset of the paroxysm, the last dose being timed for administration six hours before the shivering begins. The more soluble salts, such as the hydrochloride or hydrobromide, should be given on an empty stomach and in solution; in cases in which this procedure produces digestive disturbance, a less soluble salt, such as the sulphate or tannate, may be tried, and given after a light meal. By this means the mucosa is less irritated, but absorption is necessarily slower (MacGilchrist). As a rule this treatment does not prevent the attack from occurring, but it causes the maximum destruction of enhæmospores, and may effectually stop recurrences. In all cases, however, the drug should be continued in smaller doses after the fit. It should be remembered that quinine salts are not well tolerated in a solid form, such as pills or capsules, and that small divided doses at frequent intervals are not so efficacious as larger ones twice or thrice daily. A little opium may be combined with the quinine if nausea or vomiting are troublesome. In severe cases, and in the autumno-æstival type, due to the *Hæmomonas præcox*, larger doses and more prolonged treatment is necessary.

In infancy one or two grains of a soluble salt, such as the acid hydrochloride, may be given by the mouth, dissolved in water, or double this amount *per rectum*, in thin gruel (Holt). The dose in either case may be given every four or six hours. Older children require larger doses, and at ten years adult doses are usually necessary. At any age above infancy it may be necessary to disguise the bitter taste, or to employ one of the less soluble salts, such as the tannate. Some authors recommend the latter concealed in chocolate.

When, owing to intolerance by the stomach, quinine cannot be given by the mouth, and also

in very severe cases where an immediate or powerful effect is urgently necessary, the question of subcutaneous, intramuscular or intravenous injections must be considered. The opinions of workers in tropical countries vary somewhat as to the absolute and relative advantages of these methods. Quinine salts are somewhat irritant, and liable to cause local necrosis, except in dilutions the bulk of which would render them impracticable. When intolerance is the main difficulty, it would seem preferable to employ the intramuscular method, a dose of 5 gr. or more of the acid hydrobromide being injected into the gluteal muscles, in place of the ordinary dose by the mouth.

Intravenous injections of the same salt may be given in cases of extreme severity, 7 to 10 gr. or even more being run into a vein in two or three pints of isotonic salt solution. Attention has recently been called to the clinical fact that, especially among natives in tropical countries, tetanus is occasionally known to occur during a course of treatment by means of subcutaneous or intramuscular injections of quinine. This is explained by certain experiments and observations which show that tetanus spores may remain latent for long periods in the body, and possibly do so in quite a large number of individuals. When, however, a focal necrosis is set up by an irritant like quinine, an anaërobic area is produced in which tetanus spores can develop with the production of active bacilli, and at the same time phagocytic action is inhibited (Semple).

In cases in which hæmoglobinuria is present, quinine should not be given unless the plasmodia can be demonstrated in the blood. Some think that the alkaloid itself is preferable in this condition, which, as is well known, has been attributed, with rather unfortunate results, to the drug and not to the parasite. Recent views attribute the so-called "black-water fever" to other causes than the malarial parasite, though it occurs most frequently in partially immunised persons, and where the autumno-æstival or malignant type of malarial infection is common (Deeks and James). It appears rational, therefore, to withhold quinine where the parasite is not present, but irrational to delay immunisation by means of the drug, as half measures may fail to prevent malaria, and predispose to the hæmoglobinuric infection.

Recurrence in spite of treatment is generally due to insufficient dosage, or to the individual doses being too small. The spores, like other living organisms, have a certain power of acquiring tolerance to the drug, and this is most likely to occur if they are exposed to small quantities at repeated intervals. The rule, then, should be to make the doses as large as possible, and to allow a sufficient interval between them.

Salts of Quinine.—The hydrochloride or hydrobromide are probably the most useful salts of quinine; the sulphate is too insoluble and the acid sulphate, though soluble, contains rather a low percentage of quinine, and is highly acid and consequently more irritant.

In the following table the various salts which have been used in medicine are arranged according to their solubility in water. The content in anhydrous quinine is given in the second column, the solubility in alcohol in the third, and the doses in the fourth.

Salt.	Solubility in Water.	Per cent. Alkaloid.	Solubility in Alcohol.	Dose.	
Cacodylate (B.P.C.)	very	—	freely	15–60 mg.	$\frac{1}{4}$–1 gr.
Acid hydrochloride (B.P.)	1 in 0·75	71·86	1 in 5	0·5–6 dg.	1–10 gr.
Lactate (B.P.C.)	1 in 6	78·26	very soluble	0·5–3 dg.	1–5 gr.
Acid hydrobromide (B.P.C.)	1 in 7	60	easily	0·5–6 dg.	1–10 gr.
Acid sulphate (U.S.P.)	1 in 10	59·12	1 in 10	0·5–6 dg.	1–10 gr.
Formate (B.P.C.)	1 in 19	87·56	soluble	0·5–6 dg.	1–10 gr.
Acid hydriodide (B.P.C.)	1 in 20	48·4	—	0·5–3 dg.	1–5 gr.
Hydrochloride (B.P., U.S.P.)	1 in 40	81·73	1 in 1	0·5–6 dg.	1–10 gr.
Hydrobromide (U.S.P.)	1 in 55	76·6	1 in 0·7	0·5–6 dg.	1–10 gr.
Valerianate (B.P.C.)	1 in 120	72·97	1 in 2	0·5–2 dg.	1–3 gr.
Glycerophosphate (B.P.C.)	1 in 200	72·64	1 in 40	0·5–6 dg.	1–10 gr.
Hypophosphite (B.P.C.)	1 in 250	83·07	1 in 40	0·5–3 dg.	1–5 gr.
Acetylsalicylate (B.P.C.)	1 in 350	64	1 in 50	0·5–3 dg.	1–5 gr.
Benzoate (B.P.C.)	1 in 350	72·65	soluble	1–6 dg.	2–10 gr.
Sulphate (B.P., U.S.P.)	1 in 800	73·55	1 in 65	0·5–6 dg.	1–10 gr.
Tannate (B.P.C.)	1 in 800	—	1 in 30	0·5–6 dg.	1–10 gr.
Citrate (B.P.C.)	1 in 1200	72·5	1 in 45	0·5–6 dg.	1–10 gr.
Arsenate (B.P.C.)	sparingly	64	—	4–8 mg.	$\frac{1}{16}$–$\frac{1}{8}$ gr.
Ethylcarbonate (B.P.C.)	sparingly	—	easily	0·5–6 dg.	1–10 gr.
Alkaloid (U.S.P.)	slightly	—	1 in 1	0·5–3 dg.	1–5 gr.
Hydriodide (B.P.C.)	slightly	71·71	freely	0·5–3 dg.	1–5 gr.
Salicylate (U.S.P)	very slightly	68·79	1 in 24	0·5–3 dg.	1–5 gr.
Iodohydriodide (B.P.C.)	insoluble	45·9	insoluble	0·5–2·5 dg.	1–4 gr.
Hydrofluoride (B.P.C.)	insoluble	94·17	soluble	6–12 cg.	1–2 gr.

6. Synthetic Quinine Compounds.—Derivatives of quinoline were introduced many years ago as substitutes for quinine, such as thalline, kairoline, kairene, analgene and thermifugine. They are all too toxic for practical purposes and are liable to cause hæmoglobinuria and other undesirable effects. They have now been abandoned. A large number of newer bodies have, however, been introduced and found some vogue; two objects have been aimed at in these compounds, namely, to eliminate the unpleasant bitter taste of quinine salts, and to produce an unirritating soluble substance for hypodermic use. These two qualities, however, are not to be obtained together, for the bitter taste of quinine derivatives can only be avoided by using insoluble or little soluble compounds.

It may be said generally that these compounds have not found much favour with the profession, apparently because the disadvantage they were supposed to remedy is not really a very serious one. Euquinine has perhaps had the greatest vogue, and recently quinine and urea hydrochloride has been employed rather largely, though only for a special purpose.

I. Insoluble Substances

1. *Euquinine* ($C_2H_5COO.Q$) is the propionic acid ester of quinine. It contains about 81 per cent. of the alkaloid, and is not decomposed in the stomach. The dose is 5 to 15 gr. (0·3–1 gm.) once or twice daily, the latter quantity being suitable for malarial cases, and representing about 12 gr. of the alkaloid. In spite of its insolubility, however, it may cause gastric irritation and tinnitus in some cases. It is slightly bitter.

2. *Aristoquin* $\left(CO{<}\begin{matrix}O.Q\\O.Q\end{matrix}\right)$, the carbonic acid ester of quinine, is quite insoluble, and so tasteless. It contains about 96 per cent. of the alkaloid. It is decomposed in the stomach, and may give rise to the usual symptoms of cinchonism. The dose is the same as that of euquinine, but the alkaloidal content is higher.

3. *Saloquinine* $\left(C_6H_4{<}\begin{matrix}OH\\COO.Q\end{matrix}\right)$ is the salicylic acid ester of quinine. It only contains 68·5 per cent. of the alkaloid. It is decomposed in the stomach and may set up digestive disturbances and tinnitus, much as do more simple quinine salts. The dose is 8 to 15 gr. (0·5–1 gm.).

4. *Quinaphthol* is the sulphate of β-naphthol and quinine, and contains about 42 per cent. of the alkaloid. The dose is 8 gr. (0·5 gm.) as an intestinal antiseptic. It contains too little quinine for use in malaria, and has no advantages as an antiseptic over a mixture of the two drugs in a pill or cachet.

5. *Quinaphenin* is a compound of quinine and phenetidin ($NH_2.C_6H_4.OC_2H_5$), is almost insoluble, and contains 78 per cent. of the alkaloid. The dose is 2½ to 5 gr. (0·15–0·3 gm.). The latter will only represent 3·8 gr. of quinine. Larger doses are not to be recommended, owing to the toxic nature of phenetidin. It is, therefore, a useless compound, for small doses of quinine are mainly valuable as bitters.

6. *Insipina* is an ester of quinine sulphate with diglycolic acid $\left(O{<}\begin{matrix}CH_2COOH\\CH_2COOH\end{matrix}\right)$, and contains 72·2 per cent. of the alkaloid. It is insoluble and tasteless. The dose should be half as large again as that of the hydrochloride; it appears to have no more toxicity than ordinary quinine salts, but it is easily decomposed and must be protected from light. It is thus unsuitable for use in tropical climates.

7. *Aurochin* is an ester of quinine and *para*-amido benzoic acid ($NH_2.C_6H_4.COOH$). It is not very soluble, and so has only a slightly bitter taste. The dose is one quarter larger than quinine. It has no special advantages except those due to its insolubility.

II. Soluble Substances

Of these there are three: *Quinopyrin*, a compound of quinine hydrochloride and antipyrin, which is too toxic for general use; *Quinine-Guaiacol-sulphonate*, which is apparently intended to combine the effects of both drugs, and thus has no advantage over a mixture containing them; and *Quinine and Urea Hydrochloride*, which demands a somewhat more lengthy consideration.

It was originally intended for use in malaria and other conditions in which quinine may be given, its solubility and non-irritant character rendering it suitable for injections. Its main disadvantage is its small content of the alkaloid. The dose is 5 to 15 gr. (0·3–1 gm.). Larger doses may, however, be given with safety, and 15 to 25 gr. (1–1·6 gm.) have been administered intramuscularly and repeated in three or four hours in pneumonia, apparently with advantage to the general condition of the patients (S. S. Cohen). But it is as a local anæsthetic that this compound has gained most vogue during the last three years. Quinine itself has been known to have an anæsthetic action for some five or six years; a 0·5 per cent. solution has been injected into the nerves and tissues of an amputation stump to lessen post-operative pain (Pleth). A coagulable exudation forms in the tissues and there may be some reddening of the skin, but no further inflammatory symptoms occur. Temporary anæsthesia appears almost at once, and if the solution is retained it may last several days.

Quinine and urea hydrochloride is similarly employed in 1 per cent. solution by a method of infiltration. The solution should be boiled

before use. The anæsthesia begins in about ten minutes and lasts several hours; it may continue for some days. There is some hæmostatic action, and no toxic symptoms have as yet been observed.

Ethyl-Hydro Cupreine.—Cupreine, or hydroxy-cinchonine, is an alkaloid obtained from a species of Remijia, a group of plants closely related to cinchona. Its formula differs from that of quinine in that one methoxy (OCH_3) group is replaced by hydroxyl (OH), and may be represented as $C_{19}H_{20}N_2OH.OH$. It is only half as toxic as quinine, owing to the absence of the methoxy group, which apparently has "anchoring" functions. Ethyl-hydrocupreine, $C_{19}H_{22}N_2.OH.OC_2H_5$, has been found experimentally to have a protective and curative action in the pneumococcal infections of mice (Morgenroth). A few cases have been reported of its action on human beings suffering from pneumonia (Vetlesen). Three doses of 8 gr. (0·5 gm.) were given in twenty-four hours. The cases were all in an early stage, and the results were on the whole encouraging, as in most the temperature fell early, but as there is no means of telling how long any case of pneumonia will last it is impossible to say whether the result was due to the drug or not. One case, which is described as a very virulent infection, did not terminate till the eighth day. That the drug possesses some of the usual cinchona attributes was shown by the occurrence of temporary deafness and tinnitus in two out of nine cases. A case of pulmonary tuberculosis and one of endocarditis were uninfluenced by the drug.

[Its effect on the isolated heart appears to be definitely injurious.—Ed.]

A combination of treatment by ethyl-hydrocupreine and antipneumococcic serum may, perhaps, yield improved results.

Preparations

CINCHONA.

(A) B.P. Preparations.

Cinchonæ Rubræ Cortex contains 5 to 6 per cent. total alkaloids, one-half of which are quinine and cinchonidine.

Extractum Cinchonæ Liquidum contains 5 per cent. alkaloids.
Dose: 5–15 min. (3–10 dl.).

Tinctura Cinchonæ contains 1 per cent. alkaloids.
Dose: ½–1 fl. dr. (2–4 ml.).

Tinctura Cinchonæ Co. contains 0·5 per cent. alkaloids, also bitter orange peel and serpentary.
Dose: ½–1 fl. dr. (2–4 ml.).

Infusum Cinchonæ Acidum contains also aromatic sulphuric acid.
Dose: ½–1 fl. oz. (15–30 ml.).

(B) B.P.C. Preparations.

Decoctum Cinchonæ (B.P., 1885).
Dose: ½–2 fl. oz. (15–60 ml.).

Elixir Cinchonæ (made from yellow calisaya) contains aromatics.
Dose: ½–1 fl. dr. (2–4 ml.).

Glycerinum Cinchonæ contains 1 per cent. total alkaloids.
Dose: ½–1 dr. (2–4 ml.).

Mistura Cinchonæ Acida contains 10 min. each of the liquid extract of cinchona and dilute nitric acid, and 30 min. of aromatic syrup to the ounce.
Dose: ½–1 fl. oz. (15–30 ml.).

Vinum Cinchonæ. 1 part of the Elixir in 8.
Dose: ½–1 fl. oz. (15–30 ml.).

Vinum Cinchonæ Ferratum contains 5 parts of iron and ammonium citrate in 100 parts of Vinum Cinchonæ.
Dose: ½–1 fl. oz. (15–30 ml.).

(C) U.S.P. Preparations.

Cinchona. The bark of various species of cinchona yielding not less than 5 per cent. total alkaloids and 2·5 per cent. quinine.

Fluidextractum Cinchonæ.
Dose: 1 fl. dr. (4 ml.).

Tinctura Cinchonæ.
Dose: 1–4 fl. dr. (4–16 ml.).

Tinctura Cinchonæ Co. Red cinchona with sepentary and bitter orange peel.
Dose: 1–4 fl. dr. (4–16 ml.).

QUININE AND ITS SALTS.

(A) B.P. Preparations.

The hydrochloride, sulphate, acid hydrochloride, *Dose* 1–10 gr. (6–60 cg.), and the citrate of iron and quinine, *Dose* 5–10 gr. (3–6 dg.).

Tinctura Quininæ (Hydrochloride). Flavoured with orange.
Dose: ½–1 fl. dr. (2–4 ml.).

Tinctura Quininæ Ammoniata (Sulphate).
Dose: ½–1 fl. dr. (2–4 ml.).

Pilula Quininæ Sulphatis.
Dose: 2–8 gr. (12–50 cg.).

Vinum Quininæ (Hydrochloride).
Dose: ½–1 fl. oz. (16–30 ml.).

Syrupus Ferri Phosphatis cum Quinina et Strychnina. Easton's Syrup. Each fluid drachm contains $\frac{4}{5}$ gr. quinine sulphate and $\frac{1}{32}$ gr. strychnine.
Dose: ½–1 fl. dr. (2–4 ml.).

(B) B.P.C. Preparations.

Oleinatum Quininæ. 25 per cent. quinine in oleic acid (by weight).

Granulæ Quininæ Citratis (effervescent).
Dose: ½–1 fl. dr. (2–4 ml.).

Syrupus Quininæ Hydriodidi contains 1 gr. of the acid hydriodide to the drachm.
Dose : ½–1 fl. dr. (2–4 ml.).

Syrupus Quininæ Hydrobromidi contains 1 gr. of the acid hydrobromide to the drachm.
Dose : ½–1 fl. dr. (2–4 ml.) in water.

Lotio Quininæ. A hair-wash containing 0·11 per cent. of quinine hydrochloride.

Pessus Quininæ contains 3 gr. of quinine hydrochloride.

Syrupus Hypophosphitum Co. contains quinine hypophosphite.
Dose : 1–2 fl. dr. (4–8 ml.).

Granulæ Quininæ Salicylatis (effervescent) contain 2 per cent. of the salt.
Dose : 60–120 gr. (4–8 gm.).

Elixir Quininæ Ammoniatum contains half the amount of quinine sulphate present in the ammoniated tincture, and is more palatable.
Dose : ½–2 fl. dr. (2–8 ml.).

Elixir Quininæ Ammoniatum Co. is the same strength as the ammoniated tincture.
Dose : ½–1 fl. dr. (2–4 ml.).

Liquor Quininæ et Strychninæ contains 34 gr. quinine sulphate, 1⅓ gr. strychnine, and 16 min. concentrated phosphoric acid in 1 fl. oz.; used for making Easton's Syrup : 1½ volumes to 1 volume ferrous sulphate and syrup up to 8 volumes.

Mistura Quininæ contains 1 gr. of quinine sulphate to the ounce.
Dose : ½–1 fl. oz. (15–30 ml.).

Mistura Quininæ cum Ferro contains 1 gr. quinine sulphate and 10 minims Liquor Ferri Perchloridi to 1 fl. oz.
Dose : ½–1 fl. oz. (15–30 ml.).

Pilula Quininæ Sulphatis cum Ferro contains 1 gr. quinine sulphate and 1 gr. exsiccated ferrous sulphate.
Dose : 1 or 2 pills.

Pilula Quininæ Sulphatis Co. contains ½ gr. quinine sulphate, ⅓ gr. reduced iron, $\frac{1}{100}$ gr. arsenious anhydride and $\frac{1}{100}$ gr. strychnine with extract of gentian.
Dose : 1 or 2 pills.

Tablettæ Quininæ contain 1 gr. each.

Tablettæ Quininæ Sulphatis et Ferri contain 1 gr. each of quinine sulphate and exsiccated ferrous sulphate.
Dose : 1–3 tablets.

(C) U.S.P. Preparations.

The alkaloid, the sulphate, the acid sulphate, the hydrobromide, the hydrochloride, the salicylate—*Average Dose* 4 gr. (2·5 dg.)—and also the citrate and soluble citrate of iron and quinine—*Average Dose* 4 gr. (2·5 dg.)—are official. Also the following preparations—

Oleatum Quininæ (oleinatum).

Syrupus Ferri, Quininæ et Strychninæ Phosphatum.
Dose : 1 fl. dr. (4 ml.).

Elixir Ferri, Quininæ et Strychninæ Phosphatum.
Dose : 1 fl. dr. (4 ml.).

Glyceritum Ferri, Quininæ et Strychninæ Phosphatum.
Dose : 15 min. (1 ml.).

Syrupus Hypophosphitum Co. contains quinine.
Dose : 2 fl. dr. (8 ml.).

Cinchonine.
The sulphate (*Dose*, 8–12 gr., 5–12 dg.).
Average Dose : 4 gr. (2·5 dg.).

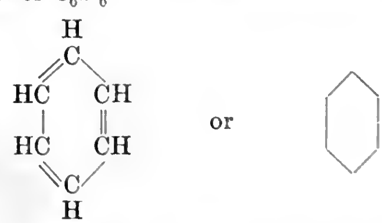
Cinchonidine.
The sulphate (*Dose*, 8–20 gr., 5–12 dg.).
Average Dose : 4 gr. (2·5 dg.).

Note.—The many preparations of cinchona are now practically obsolete and might with advantage be omitted. The Elixir, pleasant bitter, and the Compound Tincture might perhaps be retained as stomachics. Cinchonine and cinchonidine are also no longer used, and should be omitted.

J. M. F.-B.

COAL-TAR DERIVATIVES

The destructive distillation of coal, undertaken on a commercial scale for the production of illuminating gas, gives rise to a series of hydrocarbons characterised by the presence of a ring structure, the simplest of which is benzene or benzol C_6H_6—



Owing to the peculiar odour of many of these derivatives, they are known collectively as the "aromatic" compounds, as distinguished from the "aliphatic" or "fatty" hydrocarbons which have simple chains of linked carbon atoms.

There are general physiological characteristics of each of these two series. Lauder Brunton has indicated these by stating that the aliphatic derivatives act mainly on the sensory cells, producing excitement followed by anæsthesia ;

the aromatic bodies, on the other hand, act mainly on the motor cells, producing convulsions and paralysis.

Benzene itself belongs to the so-called "catalytic" poisons; that is, small amounts so act on the labile protoplasmic molecule as to check or arrest the complex chemical processes which underlie its activity. It is thus a *protoplasmic poison.*

If frogs are placed in half a litre of water containing five drops of benzene they show in ten minutes increased reflex irritability, and soon after symptoms of *paralysis* (Loew).

In cases of poisoning by benzene in man the chief symptoms are *convulsions, coma, cyanosis,* and the appearance of *methæmoglobin* in the blood and urine. Purpuric rashes occur in some cases, and hæmorrhages from the mucous membranes.

Naphthalene, the next higher hydrocarbon of the aromatic series is less toxic. Its action is similar, and it has been observed to act as an *antipyretic.*

Nitrobenzene, $C_6N_5NO_2$, also produces toxic symptoms of the same character. A small quantity placed on the tongue causes *numbness.*

These properties seen in the simplest members of the aromatic series are transmitted in varying degrees to their more complicated derivatives. By the addition of "side chains" to the benzene ring some of these actions can be increased or diminished or even abolished altogether. Thus a large series of drugs of varying utility can be produced, which do not indeed show any new pharmacological activities, but which display one or more of the original benzene actions to a greater or less degree.

Speaking generally, the hydroxyl derivatives of benzene are more powerful protoplasmic poisons, whereas those containing a nitrogen group and no unsubstituted hydroxyl have a specific action in lowering febrile temperatures and abolishing certain kinds of pain.

Two of the simplest benzene derivatives are hydroxybenzene C_6H_5OH or phenol, and amidobenzene $C_6H_5NH_2$ or aniline. From these, two large classes of drugs have been evolved, the antiseptics and the antipyretics.

The Aromatic Antiseptics

A distinction must always be drawn between antiseptic action, by which is meant the inhibition of the growth of micro-organisms, and disinfectant or germicidal action, by which the actual destruction of the living germs is accomplished. Most of the substances commonly employed exhibit both these actions under appropriate conditions, but not always with equal certainty. Paul and Krönig stated that the inhibitory power of a substance depends directly on the concentration of the solution, whereas its bactericidal power depends on the length of time during which it acts; it has been shown that staphylococcus aureus is killed by a 1 per cent. solution of terpineol (an isomer of borneo camphor) after five hours; the same strength solution of *ortho*-xylenol (a dimethyl phenol) killed it in thirty seconds. Terpineol, however, completely inhibited its growth in 1 in 15,000 solution, whereas *ortho*-xylenol required a strength of 1 in 7000 to produce this effect.

Again, various organisms behave differently to the same antiseptic. The growth of the diphtheria bacillus has been found to be much more easily inhibited by thymol than that of the staphylococcus.

Increase in the strength of a solution does not always mean a proportionate increase in germicidal power. A 0·5 per cent. solution of thymol kills staphylococci in five minutes, but a 5 per cent. solution takes two minutes, and not half a minute, as might have been expected. Most disinfectants are relatively more efficient in a dilute than in a strong solution.

The Standardisation of Disinfectants.—In 1903 Rideal and Walker published a method for comparing the germicidal power of disinfectants which has been widely adopted and considerably criticised, but which, within certain limits, and perhaps with certain modifications, affords a valuable means of estimating the capabilities of any given substance. The principle on which the test was devised was to eliminate, as far as possible, all the factors which might vary the potency of the disinfectant tested, so that it could be compared justly with a standard disinfectant which was tested under the same conditions. Briefly, the method consists in adding a given amount (5 drops) of a twenty-four hours' culture of B. typhosus in broth, to 5 c.c. of the disinfectant to be tested, dissolved in distilled water in various strengths, and to several tubes of standard phenol solutions of similar bulk. These are sub-cultured into broth tubes at certain intervals, so that the disinfectant is allowed to act on the organisms for definite periods, varying from two and a half to fifteen minutes. The strength of the disinfectant required to kill the organism is compared to the strength of phenol solution which kills it in the same interval of time, and expressed as a fraction, the numerator of which is the dilution of the disinfectant and the denominator that of the phenol solution. This is known as the "carbolic acid coefficient."

This method has been criticised on various grounds. It has, in the first place, given variable results in the hands of different workers of

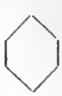
presumably similar technical ability. In the second place it takes no account of the practical use of disinfectants, which are nearly always employed in the presence of organic matter and not merely in distilled water. In the third place the method of determining the coefficient has been thought to be faulty, or at any rate capable of improvement.

Thus it has been proposed to add such organic matter as milk, urine, or ground-up dried fæces to the solution to be tested, and considerable technical modifications of the Rideal-Walker method were suggested by the *Lancet* commissioners in 1909, and approved by many important authorities.

The Effect of Organic Matter.—Martin and Chick, experimenting with dried, powdered fæces, found that the presence of this organic matter inhibited the action of phenol solutions to a much less extent than that of the emulsions of phenols or the so-called "phenoloids," and that the finer the emulsion the greater was the loss of germicidal power. On the other hand, in the absence of organic matter the emulsified preparations are more efficient than the solutions. This they explained on physico-chemical grounds, showing that the drops in the emulsified bodies absorbed the organic matter and so failed to act on the organisms, while in the absence of the former they absorbed the organisms themselves, and so were more efficient than simple solutions.

Mechanism of Action.—How the aromatic germicides act, that is, by what particular mechanism they kill the germs, is not definitely known. The absorption of the chemical substance by the bacterial cell appears to be the first step, and conditions which interfere with this will diminish the efficacy of the disinfectant, and *vice versâ*. When the phenolic substance has entered the cell it apparently does not combine chemically with its protoplasm, but appears to precipitate it as soon as a certain concentration is reached, much in the same way that heat coagulates egg albumin, or salt solutions precipitate globulins.

Chemical Structure.—The chemical relationships of the principal aromatic antiseptics will be easily understood from the following table—

1. Benzene C_6H_6 

(*a*) Phenol

Oxybenzene, carbolic acid

OH

Benzoic acid

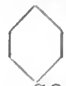
COOH

Cinnamic acid

CH:CH.COOH

Sodium Sulphocarbolate

ONa



SO_2OH

Zinc Sulphocarbolate

O — Zn — O

$SO_2.OH$ $SO_2.OH$

(*b*) Dioxybenzenes

Pyrocatechin (ortho)

OH

OH

Resorcin (meta)

OH

OH

Hydrochinone (para)

OH

OH

Guaiacol (Monomethyl Ether of Pyrocatechin)

OH

OCH_3

(*c*) Trioxybenzenes (only one of importance)

Pyrogallol (Pyrogallic acid)

OH

OH

OH

2. Toluene $C_6H_5CH_3$

CH_3

(*a*) Cresols (oxytoluenes).

(ortho)

CH_3

OH

(meta)

CH_3

OH

(para)

CH_3

OH

(*b*) Dioxytoluenes (one isomer only of importance)

Homopyrocatechin

CH_3

OH

OH

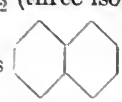
Creosol (monomethyl ether of homopyrocatechin)

CH_3

OCH_3

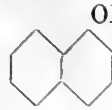
OH

3. Xylenes $C_6H_4(CH_3)_2$ (three isomers).

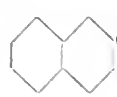
4. Naphthalene $C_{10}H_8$ 

α-naphthol

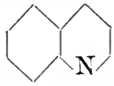
OH



β-naphthol



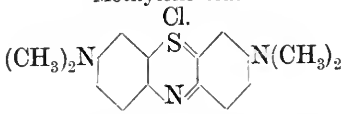
OH

5. Quinoline C_9H_7N 

Chinosol, a potassium salt of oxyquinoline sulphate, or a mixture of oxyquinoline and potassium sulphates.

6. Organic dye stuffs.

Methylene blue



Trypan red } Contain sulphur.
Trypan blue }
Malachite green G
Methyl Violet.

The chemical structure of these dyes is too elaborate for reproduction in this article. A short résumé of the chemistry of these bodies will be found in the *Chemical Basis of Pharmacology*, by Prof. Francis and the writer, published by Arnold.

Pharmacology and Therapeutic Uses of the Aromatic Antiseptics

These substances are used both internally as gastro-intestinal, urinary and respiratory antiseptics, and externally in certain diseases of the skin. They are also largely employed in surgery for preventing the growth of germs near wounds or instruments and dressings. In the following account of this group, phenol and the substances usually employed as surgical and general disinfectants and antiseptics, will first be described, then those specially intended for internal medication, and lastly those used in dermatology. This, however, is only a rough grouping for convenience in description, and it will be seen, especially in the lists of preparations, that many substances are used for more than one purpose, and might be included in more than one group.[1]

Phenol (Carbolic Acid).—In very small amounts phenol is said to increase cellular activity, but in larger quantities it is inhibitory and eventually lethal. Its antiseptic action is generally well marked in 5 per cent. solution, but varies with the organism attacked.

Spore-bearing organisms are the most resistant, and the pyogenic cocci are more resistant than the pathogenic bacilli of the typhoid group. The virulent strains are perhaps rather more difficult to kill than non-virulent strains of the same organism.

[1] Editorial Note.—Benzene, otherwise called Benzol, C_6H_6, has been recently used in the treatment of leukæmia (*q.v.*).

The action of phenol is much increased by warmth. Solutions (0·5 per cent.) which failed to kill typhoid bacilli in fifteen minutes at 22° C., killed them in five minutes at 40° to 44° C. The addition of sodium chloride, 4 per cent. added to a 5 per cent. phenol solution, greatly increased its disinfectant action on anthrax spores. Alcohol diminishes the action of phenol; a solution in absolute alcohol has little germicidal power.

The reason for this is that sodium chloride and other electrolytes decrease the concentration of phenol in water, so that more goes into the bacterial bodies. Fats, oils and glycerine, almost prevent the germicidal action of phenol (except lanolin). Carbolic acid is incompatible with soap, so that carbolic soaps are worthless as disinfectants (Hewlett, *Milroy Lectures*, 1909).

When taken into the animal body, phenol in strong solution acts as a violent caustic poison, producing collapse and death very rapidly. In small doses it acts as a gastric antiseptic, and is rapidly absorbed. It probably circulates as phenyl sulphuric acid $C_6H_5O.SO_2.OH$ and is mainly excreted in the urine in this form. Some of it is also combined with glycuronic acid, and small amounts are oxidised to pyrocatechin and hydrochinone, which are excreted in combination with the same acids. The presence of these bodies gives the urine a "smoky" appearance.

Doses large enough to cause toxic symptoms, but not strong enough to produce severe local damage to the gastric mucosa cause nausea, followed by drowsiness deepening to coma, sometimes twitching or convulsions and transient acceleration of pulse and respiration rate, followed by failure of both. Respiratory failure is caused by depression of the medullary centres, cardiac failure probably by local action on the heart muscle. There is some dilatation of the cutaneous vessels and a fall of temperature.

The urine is darkened and smoky owing to the presence of the oxidation products of phenol; blood and albumen may occur as the result of acute nephritis set up by these bodies. The treatment of carbolic acid poisoning consists in giving white of egg and alcohol by the mouth together with suspensions of lime, to combine with or dilute the poison in the stomach. The stomach-tube, if used, must be cautiously applied, owing to the possibly damaged state of the stomach-walls. Stimulants hypodermically, as well as warmth and artificial respiration, are indicated. There is some theoretical ground for injecting sodium sulphate intravenously, as the poison is excreted in a comparatively inert form combined with sulphur.

Phenol is still employed to some extent in ulcerative conditions of the stomach and

duodenum, and as a gastric antiseptic. It may be employed as a caustic and anæsthetic to the skin; a little carbolic acid on wool is a common application to the cavity of an aching tooth.

Crude phenol, containing cresols and other analogous substances, and also creosote, are used in pulmonary diseases, especially bronchiectasis, to disinfect the respiratory tract. The patient is placed in a small chamber, his eyes being carefully protected, and the substance is volatilised by heat, giving off dense fumes which the patient inhales. More elegant preparations (cresoline etc.) are used as inhalations in whooping cough, and apparently do good.

Glycerine of carbolic acid is used as an antiseptic mouth-wash (15 min. to 1 oz., about 3·5 per cent.), and is applied to the skin in parasitic diseases (tinea) either pure or diluted.

The germicidal action is too feeble to make these preparations of much value.

Carbolic acid lotion used for surgical purposes is usually 5 per cent., and is often coloured pink.

Other Aromatic Disinfectants

Those intended primarily for the disinfection of external objects fall into four groups.

1. **The Cresols.**—These are more powerful germicides than phenol under certain conditions, but they are insoluble and have to be specially treated to render them practically useful. The more important are—

(a) *Liquor Cresolis Saponatus* (B.P.) contains 50 per cent. cresol emulsified in potassium hydroxide and castor oil.

(b) *Liquor Cresolis Co.* (U.S.P.) is 50 per cent. cresol emulsion in alkali and linseed oil. The emulsion is not very satisfactory, and on dilution considerable separation of the oil occurs. Liquor Cresolis Saponatus (B.P.C.) is better.

(c) *Jeyes' Fluid* is an emulsion of cresols in resin soap. It forms a clear solution when diluted with water.

(d) *Lysol* is a strongly alkaline solution of cresols and higher homologues (50 per cent.).

2. **The Phenoloids.**—This name is given to a number of oxidised hydrocarbons obtained from distillation of coke. They are the principal constituents of—

(a) *Cyllin*, said to contain 60 per cent. phenoloids mainly with a diphenyl nucleus, and under 3 per cent. of phenols.

(b) *Izal* is obtained from the so-called tar-oil. It is said to be mainly phenoloid.

(c) *Kerol* is a similar substance, said to contain no phenol or cresol.

3. **Quinoline Compounds.**—This class only contains one example—

Chinosol, which is less toxic than phenol, easily soluble in water and not caustic. It may also be used internally. A one *per mille* solution makes an excellent mouth-wash or solution for syringing a septic throat. It is not suitable for instruments, as it turns them black if they are left in the solution for any time.

4. **Xylene.**—The ordinary xylol, a mixture of homologous xylenes, is not used for ordinary disinfection, but small quantities may be poured over solutions of organic material to prevent decomposition. Its main use is in laboratory experiments.

Comparison of Aromatic substances used as "Disinfectants."—While the carbolic acid coefficient, carefully determined by experts of known ability, and perhaps with certain modifications in technique, is a valuable guide to the efficacy of a disinfectant, due regard must be had to the purpose for which the disinfectant is required.

1. If the organism is known, the carbolic acid coefficient for that organism should be ascertained.
2. If the disinfectant is to act in the presence of organic matter (*e. g.* fæces) the solutions will act better than the emulsions, and fine emulsions better than coarse, imperfect ones. Hence the miscibility of the emulsion with water is of importance.
3. The toxicity of the disinfectant must be considered if it is to be largely used and placed, perhaps, in the hands of uneducated persons. Generally speaking, the phenoloid bodies are less toxic than cresol and phenol solutions.
4. If materials such as linen or other fabrics are to be disinfected, the staining or disintegrating action on these must be taken into account. The phenoloids here again present advantages.
5. The action on the skin of those handling the disinfectant should not be destructive. Phenol and strongly alkaline solutions such as lysol are, therefore, unsuitable.
6. The cost of the disinfectant is of considerable importance when more than very small quantities have to be used.

Preparations

Acidum Carbolicum (B.P.), *Phenol* (U.S.P.). Colourless deliquescent crystals turning pink on exposure to air. Soluble in 12 parts of water.
Dose: 1–3 gr. (6–20 cg.).

Acidum Carbolicum Liquifactum (B.P.), Phenol Liquifactum (U.S.P.). 100 parts of pure carbolic acid with 15 parts of water.
Dose: 1–3 min. (6–18 cl.).

Glycerinum Acidi Carbolici (B.P.). 20 per cent.

Glyceritum Phenolis (U.S.P.). 20 per cent. carbolic acid in glycerin.
Unguentum Acidi Carbolici (B.P.). 3 per cent.
Unguentum Phenolis (U.S.P.). 3 per cent. in paraffin wax.
Trochiscus Acidi Carbolici (B.P.). Containing 1 gr. (0·06 gm.) in a basis composed of gum acacia, tragacanth, lemon juice and sugar.
Suppositoria Acidi Carbolici (B.P.). Containing 1 gr. (0·06 gm.) in beeswax and oil of theobroma.

The following B.P.C. preparations are classified under the purposes for which they are intended.

1. *Surgical Lotions and Dressings.*

Lotio Acidi Carbolici. 1 in 20.
Solvellæ Acidi Carbolici. 5 gr.
Solvellæ Acidi Carbolici Fortes. 20 gr. These solid preparations are apt to deliquesce.
Carbasus Acidi Carbolici. Gauze. 5 per cent.
Gossypium Carbolisatum. Wool. 5 per cent.
Linteum Acidi Carbolici. Lint. 5 per cent.
Stupa Carbolisata. Tow. 5 per cent.
Stupa Carbolisata Co. Tow. 10 per cent.

2. *For Mouth-Washes and Disinfectants.*

Gargarisma Acidi Carbolici. Glycerin of phenol. 5 per cent.
Liquor Potassii Carbolatis Co. Liquified phenol 5 per cent., with potassium hydroxide, eau de Cologne, gluside, quillaia, chloroform, carmine and rose water. One or two tea-spoonfuls in a tumblerful of water.
Liquor Sodii Carbolatis Co. Phenol 3·125 per cent., with sodium hydroxide, orange-flower water, rose water, glycerin and tincture of cudbear. One fluid drachm to a wineglassful of water.
Lotio Acidi Carbolici et Boracis. Glycerin of phenol 1, glycerin of borax 1, distilled water 8. Diluted 5–10 times before use.
Pastillus Acidi Carbolici. Contains phenol, ½ gr.

3. *Lubricants for Catheters, etc.*

Oleum Carbolicum. 5 per cent. in olive oil. *Obsolete.*
Paraffinum Carbolisatum. 3 per cent. Also intended for a dressing.
Oleum Lubricans. 5 per cent.
Pasta Lubricans. 3 per cent. Not greasy.

4. *For Filling Cavities in Aching Teeth.*

Collodium Carbolisatum. 50 per cent.
Phenol cum Camphora. Phenol 1, camphor 3. Also for wounds, burns, etc., it is not caustic.
Resina Carbolisata. Phenol 1, mastic 1, resin 2, chloroform 1.

5. *Miscellaneous.*

Buginaria Acidi Carbolici Co. (Nasal). Phenol ½ gr., boric acid 5 gr. in each.
Pessus Acidi Carbolici. 2 gr. in each.
Phenol Iodisatum. 10 per cent. For gynæcological purposes. 1 fl. dr. to the pint for a vaginal douche.
Unguentum Acidi Carbolici Co. Phenol 9, mercuric nitrate ointment 18, sublimed sulphur 4·5, olive oil by weight 9, yellow beeswax 9. A stimulant and parasiticide.
Vapor Acidi Carbolici Co. Creosote 1, oil of eucalyptus 2, oil of pine 2, phenol to 100. For inhalation.

Cresol (B.P., U.S.P.). A straw-coloured fluid containing the three isomers.
Dose: 1–3 min. (6–18 cl.).
Liquor Cresol Saponatus (B.P.). Cresol 50, castor oil 35, potassium hydroxide 8 in water to 100.
Liquor Cresolis Co. (U.S.P.). 50 per cent. cresol suspended in soap solution.
Liquor Cresolis Saponatus (B.P.C.). Similar to lysol. It mixes with water better than the Liquor Cresolis Co. 1 to 2 per cent. dilutions are used as antiseptic surgical lotions.
Vapor Cresolis Co. (B.P.C.). Creosote 1, oil of eucalyptus 2, oil of pine 2, cresol to 100. For inhalation.

Picric Acid is trinitrophenol $C_6H_2OH(NO_2)_3$; it is an exceedingly poisonous substance, setting up many of the symptoms characteristic of the benzene derivatives. In animals it causes destruction of the erythrocytes, vomiting, collapse and convulsions. It also irritates the kidney, producing nephritis. The skin and mucous membranes are stained yellow, and the urine coloured yellow or red. There is, however, no bile pigment in the urine and no real jaundice.

Picric acid occurs in yellow crystals soluble in 90 parts of water. The picrates of sodium, ammonium, etc., are all explosive bodies. It has no particular value when given internally, but has been tried in malaria, Graves' disease, and as an antipyretic. The dose is 1–5 gr. (5–30 cg.). Externally it is a valuable application for burns, especially those caused by quicklime, and it has also been used as a stimulating lotion in eczema and other skin diseases. A 5 per cent. solution has been recommended for application to sweating feet. Large raw surfaces should not be treated with picric acid, as absorption may occur and set up symptoms of poisoning.

Preparations

Acidum Picricum (B.P.).
Carbasus Acidi Picrici (B.P.C.). 3 per cent.
Lotio Acidi Picrici (B.P.C.). 1 per cent.
Unguentum Acidi Picrici (B.P.C.). 2 per cent. in soft paraffin.

All these are intended for dressings in burns, eczema, etc.

Aromatic Substances generally intended for Internal Administration

It is not possible to administer a chemical disinfectant intravenously or by any other method, which will destroy living organisms in the body without damaging to a greater extent the tissues of the host. The specific action of certain substances, such as quinine in malaria, is of a special character, and the organisms against which they are directed are not always bacteria. The use of disinfectants internally, therefore, is extremely limited, and though attempts have been made from time to time to inject antiseptics especially in phthisis and pulmonary disorders, these methods have never been widely adopted, and their efficacy and safety have never been demonstrated under strict experimental conditions.

The main use of antiseptics internally has hitherto been to check putrefactive processes in the gastro-intestinal contents, and this is what is generally understood when intestinal antisepsis is recommended.

1. **Sulphocarbolate of Soda.**—A crystalline substance soluble in water, less poisonous than phenol and excreted unchanged in the urine. It is not a particularly valuable drug.

2. **Sulphocarbolate of Zinc.**—A very soluble deliquescent substance with a slightly astringent action. It may be used for all purposes for which zinc sulphate is employed than which it is rather more antiseptic. Solutions of 1 in 500–1 in 250 have been used as urethral injections in gonorrhœa. The sulphanilate, which has similar properties, has been introduced under the name of "Nizin."

3. **Naphthol.**—Of the two naphthols, β-naphthol is generally employed, as it is thought to be less toxic. It is known to be less powerfully germicidal. It is an insoluble crystalline body resembling phenol in its action, but a much stronger antiseptic. It produces in large doses similar toxic symptoms, and in addition destroys the red blood cells. It is very liable to set up nephritis. It is usually given in cachets as an intestinal antiseptic and anthelmintic.

4. **Creosote** is a colourless oily liquid with a burning taste, and is obtained by distilling wood tar, not coal tar. Its main ingredients are guaiacol and cresols. Its action is similar to that of phenol, but it is less toxic and irritant and probably a more powerful antiseptic.

It was at one time rather largely used in phthisis as a pulmonary disinfectant. Clinically it was thought to do good, but there was little experimental evidence of its value. Recently it has been superseded by guaiacol, but pills containing one or two minims are often given for gastric flatulence.

5. **Guaiacol** is a syrupy liquid, less powerfully antiseptic than creosote. It is used as a remedy in phthisis, and, like creosote, there is clinical evidence of its value, though exactly how it influences the disease is not clear. It is given in doses of 1–5 min. (6–30 cl.). Intratracheal injections of menthol 2 gr., guaiacol 1 gr., olive oil to 1 dr., may be used in tuberculous conditions of the larynx. Its main disadvantages are its unpleasant taste, the fact that it does not mix with water, and its irritant action on mucous membranes. To obviate these a number of compounds of guaiacol have been prepared, most of which are insoluble, and, therefore, tasteless.

(a) *Guaiacol Carbonate.*—This is the most largely used of the guaiacol compounds. It is tasteless and insoluble, and may be given in phthisis in doses of 5–15 gr. (3–10 dg.) or more, in an emulsion of tragacanth or with cod liver oil emulsion. It is also largely used in rheumatoid arthritis.

(b) *Guaiacol Cinnamate* is similar to the carbonate. It is probably the best of the guaiacol compounds, as it has been shown to liberate more guaiacol in the body. It is, however, expensive.

(c) *Guaiacol Potassium Sulphonate* is soluble and given in doses of a teaspoonful to a tablespoonful. It is probably the most inert of the guaiacol compounds, and passes for the most part unchanged through the body, for it is in this form that the normal excretion of guaiacol takes place (compare phenol).

(d) The *benzoate, salicylate, camphorate* and *valerianate,* present no particular advantages. The *albuminate* is soluble in dilute alkalies.

6. **Benzoic Acid** resembles salicylic acid (*q. v.*) rather than phenol in its action, but is less irritant and fails to produce the characteristic symptoms of "salicism." It increases the polynuclear leucocytes and is excreted combined with glycocoll (CH_2NH_2COOH) as hippuric acid ($C_6H_5CO.NHCH_2COOH$). It (and also its salts) are intestinal and urinary antiseptics, and are commonly given for these purposes. It is not of much value as a substitute for the salicylates in acute rheumatism, and as it has little or no action in combining with uric acid in the tissues, it is of no value in gout. In the form of Tinct. Benzoini Co. and in the Balsams of Tolu and Peru it is a common ingredient in cough mixtures.

7. **Cinnamic Acid,** a compound of benzene with an unsaturated fatty acid (acrylic acid $CH_2:CH.COOH$) is converted into benzoic acid in the body. It is a powerful antiseptic. The sodium salt (Hetol) was introduced as a remedy for phthisis, but its value has not been demonstrated.

8. **The Organic Dye-stuffs.**—*Methylene blue* is

usually given in doses of 1–4 gr. (6–25 cg.), but much larger amounts, up to 15 gr. have been recommended in some cases. It is a mild antiseptic and diuretic, and is principally excreted by the kidney, causing the urine to become bright blue. Some is excreted with the fæces, which are also stained. It may set up gastric irritation. It is mainly used as a urinary antiseptic, but has also been given in colitis and as a parasiticide in malaria and malta fever, but it does not appear to have a constant or powerful action in these diseases.

Trypan red and other allied bodies were introduced by Ehrlich and Shiga as parasiticides in trypanosomiasis. It has mainly been employed in conjunction with organic arsenical compounds, as a supplementary drug. Ehrlich's original experimental results were not, however, confirmed by the workers in the Liverpool School of Tropical Medicine, who failed to either cure or protect animals infected with various trypanosomes.

Malachite green and *methyl violet* act somewhat similarly to methylene blue, but have never been largely used.

Preparations

Sodii Phenolsulphonas (U.S.P.). Sodii Sulphocarbolas (B.P., 1898). Colourless crystals soluble in 5 parts of water.
Dose : 5–15 gr. (3–10 dg.).

Zinci Phenolsulphonas (U.S.P.). Zinci Sulphocarbolas (B.P., 1898).
Dose : 1–4 gr. (6–25 cg.).

Naphthol (B.P.), Betanaphthol (U.S.P.). Insoluble yellowish crystals.
Dose : 3–10 gr. (2–6 dg.).

Parogenum Naphtholis (B.P.C.). 1 in 10 for use in scabies, eczema and psoriasis.

Unguentum Naphtholis (B.P.C.). 1 in 10 for similar uses.

Unguentum Naphtholis Co. (B.P.C.). Naphthol 8·55, prepared chalk 5·7, soft soap 28·5, lard 57·25, for similar uses. Also called Kaposi's ointment.

Naphthol Benzoate and Salicylate (B.P.C.).
Dose : 5–10 gr. (3–6 dg.). They are insoluble, and may be given in mucilage or cachets as intestinal antiseptics.

Creosotum (B.P., U.S.P.). A colourless, oily liquid, slightly soluble in water.
Dose : 1–5 min. (6–30 cl.).

Mistura Creosoti (B.P., 1898). Creosote 1, spirit of juniper 1, syrup 30, water 480.
Dose : $\frac{1}{2}$–1 fl. oz. (15–30 ml.). A useless preparation. Small amounts of creosote merely act as a carminative, and can be better given in pill form.

Unguentum Creosoti (B.P.). 1 in 10 in paraffin.

Parogenum Creosoti (B.P.C.). 1 in 5.

Pilula Creosoti (B.P.C.). 1 min. in each.

Spiritus Creosoti (B.P.C.). 1 in 40 as a stimulant and antiseptic expectorant.
Dose : $\frac{1}{2}$–1 fl. dr. (2–4 ml.).

Aqua Creosoti (U.S.P.). Less than 1 per cent.
Dose : $\frac{1}{2}$–2 fl. dr. (2–8 ml.). As useless as the mistura.

Guaiacol (B.P., U.S.P.). Colourless crystals or liquid soluble in 80 parts of water and in spirit.
Dose : 1–5 min. (6–30 cl.).

Guaiacol Carbonas (B.P., U.S.P.). Colourless insoluble powder.
Dose : 5–15 gr. (3–10 dg.). The official dose is very small. 15 gr. are usually given and gradually increased to 30 or 40 gr.

Nebula Guaiacolis et Mentholis (B.P.C.). Guaiacol 2, menthol 4, liquid paraffin to 100.

Parogenum Guaiacolis (B.P.C.). 1 in 5.

Guaiacol Benzoate (5–12 gr., 3–8 dg.). Camphorate (5–10 gr., 3–6 dg.), Cinnamate (5–15 gr., 3–10 dg.), Phosphate (5–10 gm., 3–6 dg.), and Valerianate (2–5 min., 1–3 dl.).

Acidum Benzoicum (B.P., U.S.P.). Colourless feathery crystals, insoluble in water, soluble in alcohol, ether, oils and alkalis.
Dose : 5–15 gr. (3–10 dg.).

Sodii Benzoas (B.P., U.S.P.). Soluble in water.
Dose : 5–30 gr. (3–20 dg.).

Ammonii Benzoas (B.P., U.S.P.). Soluble in water.
Dose : 5–15 gr. (3–10 dg.).

Lithii Benzoas (U.S.P.).
Dose : 5–15 gr. (3–10 dg.). An unnecessary preparation, as neither lithium nor benzoic acid have any influence in gout.

Trochiscus Acidi Benzoici (B.P.). $\frac{1}{2}$ gr. (0·03 gm)., in a fruit basis. A placebo.

Methylthioninæ Hydrochloridum (U.S.P.). Methylene blue. A dark blue-green powder soluble in water and spirit.
Dose : 4 gr. (0·25 gm.), 1–5 gr. (6–30 cg.).

Methyl Rosanilinum (B.P.C.). Methyl violet.
Dose : $\frac{1}{10}-\frac{1}{5}$ gr. (6–12 mg.).

Aromatic Substances generally used in the Treatment of Skin Diseases

1. **Tar.**—Two sorts of tar are employed in medicine. Coal tar or Pix Carbonis and wood tar or Pix Liquida, obtained from the distillation of the wood of various species of pines.

Coal tar contains benzene, naphthalene,

anthracene and other hydrocarbons, together with various phenols, ammonia, aniline, piperidine, acridine and sulphur-containing bodies. Its aqueous solutions are acid.

Wood tar contains toluene, naphthalene and other hydrocarbons, phenol, cresols, pyrocatechin, creosols, phlorol, etc. Its aqueous solutions are alkaline.

Tar preparations are generally used as skin applications in eczema, psoriasis, pruritus, etc. The Liquor Picis Carbonis is an official imitation of the Liquor Carbonis Detergens, a proprietary article essentially an alcoholic tar extract.

The tar preparations are not often given internally, but the syrup is a good expectorant.

Oil of Cade, a tar oil obtained from juniper, is very similar to tar in composition and action, but is a pleasanter application for the skin. An ointment made with yellow wax (equal parts) is often prescribed in psoriasis.

2. **Ichthyol** contains the ammonium salts of the sulphonic acids derived from the distillation of the bituminous shale found in the Tyrol. It is a tarry substance soluble in water, in equal parts of alcohol and ether, and miscible with glycerine and oils. Its properties do not appear to differ considerably from those of other tarry bodies, and it has been used in the same way. Its value as an internal remedy for chronic rheumatism and other conditions is very problematical. The dose is 3–8 gr. (2–5 cg.) in pills or capsules. Larger doses up to 30 gr. (2 gm.) may be given.

A number of artificial substances resembling ichthyol have been prepared; some, such as desichthyol, ichthalbin, ichthoform, are practically insoluble and free from odour or taste. Ferri-ichthyol and ichthargan are iron and silver compounds. Thiol, tumenol and petrosulphol, are manufactured by heating tar oils with sulphur. They are of no more value internally than ichthyol, and have passed out of fashion with their parent substance.

3. **Resorcin** is the least toxic of the dihydric phenols, and is probably less powerful as an antiseptic than carbolic acid, which it closely resembles. It is less irritant and caustic, but is more liable to produce convulsions. It is not now used internally, but is somewhat frequently added to hair lotions (2 gr. or 3 gr. ad 1 oz.), and is used occasionally in applications for acne (1 dr. ad 2 oz.).

4. **Pyrogallol** is too toxic for internal use. In cases of poisoning the main symptoms are those due to its action as a blood poison (methæmoglobinuria, jaundice, cyanosis), and to its irritant action on the kidneys (nephritis, uræmia). It is a powerful reducing agent and has been used in psoriasis and other skin diseases as a 5–20 per cent. ointment, but even when applied to the skin it may set up toxic symptoms.

Preparations

Pix Carbonis Præparata (B.P.). Commercial coal tar, heated to 50° C. for one hour with frequent stirring.

Liquor Picis Carbonis (B.P.). A 20 per cent. solution with tincture of quillaia, which forms a suspension on dilution with water.

Pix Liquida (B.P., U.S.P.). A blackish bituminous liquid.
Dose : 2–10 gr. (1–6 dg.) in pills.

Unguentum Picis Liquidæ (B.P., U.S.P.). Tar 70, prepared lard 5, yellow beeswax 25.

Oleum Picis Liquidæ (U.S.P.). An oily substance distilled from wood tar, containing mainly guaiacols and their derivatives.
Dose : 1–5 min. (6–30 cl.).

Syrupus Picis Liquidæ (U.S.P.).
Dose : 1–2 fl. dr. (4–8 ml.).

The following B.P.C. preparations are intended for use in chronic eczema, etc.—

Lotio Picis Carbonis. 1 in 200 (or 1 in 100). From this are prepared—
Lotio Picis Carbonis Alkalina. 0·5 per cent. with soda bicarbonate.
Lotio Picis Carbonis et Plumbi. 3 per cent. with subacetate of lead.
Unguentum Picis Carbonis. 1 in 16.
Unguentum Picis Carbonis Co. 6 per cent. with ammoniated mercury.
Liquor Picis Ligni. 1 in 20.
Parogenum Picis. 1 in 4.
Unguentum Picis Molle. 70 per cent.

The following (B.P.C.) are for wound dressings—

Carbasus Styptica. Tar gauze. 5 per cent.
Stupa Styptica. Tar tow. 10 per cent.

The following (B.P.C.) are for internal use—

Aqua Picis.
Dose : 18 fl. oz. (½ litre).

Syrupus Picis cum Codeina. Codeine 0·1, alcohol (60 per cent.) 5, syrup of tar to 100.
Dose : ½–2 fl. dr. (2–8 ml.).

Oleum Cadinum (B.P., U.S.P.). Distilled from juniper tar oil. A dark brown oily liquid. Soluble in ether and chloroform, partly soluble in alcohol, insoluble in water.

Parogenum Empyreumaticum (B.P.C.). 1 in 4.

Sapo Olei Cadini (B.P.C.). Oil of cade 1, soft soap 4, alcohol 4. For application in psoriasis.

Unguentum Olei Cadini (B.P.C.). Equal parts by weight of oil of cade and yellow beeswax. For similar purposes.

Ammonii Ichthyosulphonas (B.P.C.). "Ichthyol."
Dose : 15–30 gr. (1–2 gm.).

The following B.P.C. preparations are intended for use in skin diseases such as eczema and psoriasis.

Parogenum Ichthamolis. 1 in 10.
Unguentum Ichthamolis. 1 in 10.
Unguentum Ichthamolis Co. Ammonium ichthyosulphonate 9, precipitated sulphur 9, zinc oxide 9, starch 9, distilled water 6, resorcin 4, salicylic acid 2, naphthol 2, anhydrous lanolin ointment to 100.
Pasta Ichthamolis. 1 in 10 in jelly.
Pasta Ichthamolis Co. 1 in 4.

The following (B.P.C.) are intended for application to chilblains—

Collodion Ichthamolis. 1 in 8.
Collodion Ichthamolis cum Æthere. 1 in 4.

The following (B.P.C.) are intended for gynæcological and rectal conditions—

Pessus Ichthamolis. 10 gr. in each.
Suppositoria Ichthamolis. 3 gr. in each.

Resorcinum (B.P.), *Resorcinol* (U.S.P.). Colourless soluble crystals.
Dose : 1–5 gr. (6–30 cg.), or 45 gr. (3 gm.) in 24 hours.

The following (B.P.C.) preparations are intended for use in skin diseases, eczema, psoriasis, pruritus, acne, etc.

Pasta Resorcini. 1 in 5.
Unguentum Resorcini. 1 in 8.
Pasta Resorcini Mitis. 1 in 10.
Lotio Resorcini. 1 in 10.
Unguentum Resorcini et Bismuthi Co. 1 in 12·5. Resorcin 8, distilled water 12, zinc oxide 8, bismuth subchloride 8, birch tar oil 2·5, oil of cade 2·5, starch 20, wool fat 39.
Unguentum Resorcini Co. 1 in 12·5. Resorcin 8, distilled water 8, birch tar oil 4, zinc oxide 8, bismuth subnitrate 8, wool fat 32, soft paraffin to 100.
Unguentum Resorcini cum Amylo. 1 in 50. Resorcin 2, zinc oxide 24, starch 24, hydrous wool fat 24, soft paraffin to 100.

The following (B.P.C.) preparation is intended for use as a hair-wash—

Spiritus Resorcini. 1 in 40.

Acidum Pyrogallicum (B.P.C.), *Pyrogallol* (U.S.P.). Colourless crystals soluble in water and darkening rapidly on exposure to air or sunlight.

Unguentum Acidi Pyrogallici (B.P.C.). 1 in 8 in soft paraffin.
Unguentum Acidi Pyrogallici Co. (B.P.C.). Pyrogallic acid 5, ammonium ichthyosulphonate 5, salicylic acid 2, soft paraffin 88. For use in dermatology. Small surfaces only should be covered, for fear of absorption.
Unguentum Acidi Pyrogallici Oxidatum (B.P.C.). Oxidised pyrogallic acid 5, salicylic acid 5, hydrous wool fat 90. Does not blacken the skin, is less toxic, and more permanent than the foregoing ointment.

The Aromatic Antipyretics

The propriety of attempting to reduce a febrile temperature will depend upon two main sets of considerations, firstly our conception of the cause of the pyrexia and its effect on the condition of the patient, and secondly on our knowledge of the processes whereby the antipyretic measures we adopt will become effective.

The pyrexia or elevation of temperature is one of a number of symptoms known collectively as fever, which are due to the presence of certain foreign substances in the body fluids. These substances act on the thermotaxic centre, which is situated in the basal ganglia (probably in the corpus striatum), so that an increase in heat production is not followed by a corresponding increase in heat loss. The centre still remains sensitive, in fact there is reason to believe that in febrile conditions it is rather more sensitive than usual, but it does not react in the same measure, and the higher ratio which it maintains between heat production and heat loss results in an elevation of body temperature.

By preventing heat loss the body temperature may be maintained at a febrile level apart from the presence of toxic infection. Under these circumstances it is found that with a temperature below 104° F. phagocytosis is more active, and the production of agglutinins, antitoxins and bacterio-lysins is increased. Metabolism, on the other hand, is not affected, and there is no increased nitrogen output. Moreover no parenchymatous degeneration of the viscera occurs. Above 104° F., however, the defensive mechanisms mentioned fail, and there is a certain increase in protein destruction. The other phenomena of fever, therefore, which include certain degenerative changes in the organs, increased nitrogen output, anæmia, etc., must be attributed to the presence of toxic substances in the body and not to the rise of temperature, which is a concomitant variation from normal, of a protective nature up to a certain point. It would not, therefore, seem justifiable to attempt to reduce febrile temperatures unless they rise to about 104° F. or above.

Clinically, however, it is observed that in certain cases headache and other nervous

disturbances may occur at lower temperatures, which are relieved if antipyretic measures are adopted. The rationale of this does not seem clear, but as a clinical fact it gives proper grounds for interference and justifies a departure from the general rule just enunciated.

As to the measures which may be taken to reduce the febrile temperature, obviously the most rational will be those which are calculated to remove the cause not only of the pyrexia but of the toxic or infective condition of which it is a symptom. Thus the administration of quinine in malaria and of certain sera in other infections is secondarily antipyretic. When, however, this course is impossible, three methods are open to us, either (1) to diminish heat production, (2) to increase heat loss, or (3) to act on the thermotaxic centre in such a way that its normal ratio of reactivity is restored. The first of these indications is met by such general methods as rest in bed and restriction in diet, and also by the administration of such general protoplasmic poisons as quinine, which reduce cellular metabolism. The second is met by applying cold externally to the surface of the body. The third may be effected by the administration of a number of drugs which constitute the true antipyretics and are the subject of the present article.

The choice of one or other of these methods must to a certain extent depend on circumstances, but there is at present, at any rate in this country, a large preponderance of clinical opinion in favour of the second, namely, the application of cold to the surface of the body. Although the effect produced is somewhat transitory, it has the advantage of simplicity. Any drug introduced into the body acts in more than one way, and the antipyretics are no exceptions to this rule. Although they effect our object as far as the thermotaxic centre is concerned, they produce other effects, and many of these are very undesirable.

The main conclusions as to the indications for antipyretic treatment, therefore, may be summed up as follows—

1. In acute febrile diseases antipyretic measures are not necessary unless the temperature rises above 104° F.

2. The longer the course of the disease, the more freely may antipyretic measures be taken.

3. The best method is by giving remedies which attack the causal organisms or directly neutralise their products, but this is of limited application.

4. Failing this the next best method is the application of cold to the surface of the body.

5. Coal-tar derivatives may be used where 4 is not possible, and it may be added that they are useful in slighter febrile affections, and where their analgesic action is also of value.

Pharmacological Action. — All the aromatic antipyretics have many pharmacological properties in common; these, therefore, can be stated generally, and variations noted when the individual drugs are described.

1. **Temperature.**—The thermotaxic centre, though uninfluenced under normal conditions, is in the febrile state so acted on that it responds to the increase in heat production by a greater increase in heat loss. This is brought about by a general dilatation of the cutaneous blood-vessels, and in some cases by increased secretion of sweat. The effect is most marked in cases of remittent or intermittent pyrexia, and when the natural fall is about to take place.

2. **Pain.**—There is a well-marked analgesic action with regard to certain kinds of pain produced by these derivatives. They do not act thus in cases of severe pain due to organic lesions, and have practically no narcotic effect, but they bring about a considerable relief in various neuralgic pains, in headache and the so-called "rheumatic" pains. The analgesic action is very liable to weaken when any of these drugs is constantly taken.

3. **Nervous System.**—There is little action on the motor or sensory sides of the nervous system in man. Some antipyretics have slight local anæsthetic action. Large doses may in animals produce convulsions and paralysis.

4. **Heart.**—Acceleration followed by slowing occurs as a result of a direct local action.

5. **Absorption and Excretion.**—Absorption is rapid, but less so with the more insoluble compounds. They are excreted by the kidneys usually in twenty-four to thirty-six hours.

6. **Action on Protoplasm.**—All these bodies are protoplasmic poisons, and thus have more or less antiseptic action, but are never employed for this purpose.

7. **Metabolism.**—Medicinal doses have little or no effect.

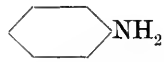
8. **Toxic Action.** — Medicinal doses of any antipyretic may in certain cases set up an irritable dermatitis with or without considerable œdema, mainly affecting the face, neck, chest and arms. Catarrh of the respiratory passages, or irritation of the gastric mucosa with nausea and vomiting, are occasionally produced. Serious collapse accompanying the fall of temperature and possibly ending in heart failure may occur, but is rare unless rather large doses have been taken. Cyanosis and the formation of methæmoglobin in the blood is more usually marked with some classes of antipyretics than others; these points will be later referred to when the individual drugs are considered.

Psychological Action. — It has been rightly pointed out that the antipyretic and analgesic

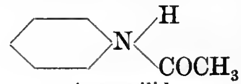
drugs do not produce a "habit" in quite the same sense as do the narcotics or hypnotics. That is to say, persons may acquire the habit of taking analgesics after long periods to free themselves from constantly recurrent pain, but no abnormal craving is established. It is merely self-medication, not morbid appetite. It is true that the dose is likely to be increased as time goes on, for the analgesic action often diminishes if repeated doses are taken, and it is only fair to this class of drug to state that by far the larger proportion of cases of poisoning occur when the medicinal dose has intentionally or accidentally been largely exceeded. This fact is well brought out by two sets of figures recently obtained in the United States.[1] A collective investigation addressed to practitioners showed that out of 814 cases of poisoning by acetanilide, antipyrin or phenacetin, there were 28 deaths and 136 cases of habitual use. Ninety-four cases occurred in children, and in nearly half the cases the drugs were taken without orders from a physician. On the other hand, inquiries addressed to 1100 hospitals and institutions, where, presumably, the drugs were always administered by the doctor's orders, and accidental over-dosage would be reduced to a minimum, there were only 31 cases of poisoning and no deaths. Ten of these cases were apparently admitted to the institutions on account of poisoning by over-dose outside. The conclusion we must draw is that, except in the relatively rare cases of special idiosyncrasy, these drugs are comparatively safe in moderate doses; but that it is never wise to start patients on a course of self-medication, especially as the dose is very likely to be increased from time to time, and that to prevent this the sale of antipyretics to the public without a recent prescription should be prohibited.

Classification of the Antipyretics. — Probably about fifty derivatives of the aliphatic series have been introduced at one time or another into medicine as antipyretics, but comparatively few of them are at all largely used, and many of them are very unsuitable for practical purposes. As their action only differs in detail, they may be most conveniently classified according to their chemical constitution into four groups.

1. **Aniline Derivatives.**—Aniline, $C_6H_5NH_2$, is a powerful antipyretic, but is far too toxic for medicinal use. In cases of poisoning by this drug, severe collapse occurs with much destruction of the red blood cells and the formation of methæmoglobin. By combining the amido group (NH_2) with other radicles, more stable substances may be produced, which are more slowly decomposed in the body and are consequently less toxic. The simplest of these is *Acetanilide*, or antifebrin—



Aniline

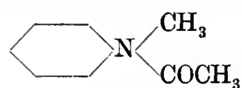


Acetanilide

in which one hydrogen alone is replaced by acetyl. Acetanilide is partially oxidised in the body into *para*-amidophenol—

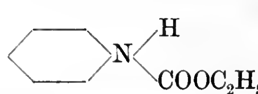
which is excreted in the urine combined with sulphuric and glycuronic acids; *para*-acetyl-amidophenol also occurs in man, but not always in other animals. It is similarly combined in the urine. Acetanilide is not easily soluble in water, and has a pungent taste. It is therefore usually given in tablets or cachets, dose, 2–5 gr. (12–30 cg.). Owing to the formation of *para*-amidophenol in the body, which is similar in its toxic action to aniline, acetanilide is liable to produce methæmoglobinæmia and collapse.

Exalgin is less toxic, as both the hydrogen atoms of the amide radicle are substituted one by methyl and one by acetyl.



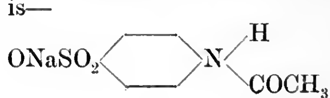
It is only slightly soluble. Dose, 1½–5 gr. (1–3 dg.). It is a powerful analgesic, but is liable to cause toxic symptoms similar to those set up by acetanilide, though not so frequently. Sodium salicylate combines with exalgin to form an inert compound, and should be given in cases of poisoning.

Euphorin (phenyl urethane, B.P.C.) is a compound of aniline and urethane. It has no hypnotic action in medicinal doses.



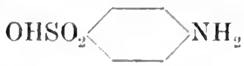
It is only slightly soluble in water and best given in dilute spirit. The dose is ¾–8 gr. (5–50 cg.), but as much as 15 gr. (1 gm.) has been given. It has no special advantages. It does not break down the red blood cells, and in toxic doses acts more like urethane.

Cosaprin is a comparatively inert body. Its structure is—



[1] Vide *Lancet*, 1909, ii, Aug. 14; and 1910, i, Feb. 12.

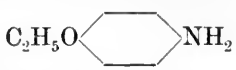
It is decomposed in the body with the formation of the inactive substance sulphanilic acid—



and is of little use as a drug.

2. *Para*-**amidophenol and Phenetidin Derivatives.**—Owing to the fact that acetanilide owes its activity to the formation of *para*-amidophenol in the body, a number of compounds of the latter substance have been investigated and found to have antipyretic and analgesic properties. Their effectiveness as drugs, and also their toxicity, will depend on the ease with which the parent substance is formed in the body, and thus it is hopeless to expect that in this class of drug a maximal therapeutic action can be combined with a minimal toxicity.

Besides *para*-amidophenol, another substance called phenetidin is formed from these derivatives. It has the formula—



and when acted on by the hydrochloric acid of the stomach, a powerfully toxic substance results—phenetidin hydrochloride. Thus derivatives of this class, which are easily broken down in the stomach, are more liable to produce toxic symptoms than the more stable compounds.

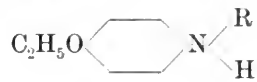
Para-amidophenol derivatives may be grouped into two classes; those which are broken down with difficulty and are consequently little toxic, and also not so powerfully antipyretic, and those which are easily broken down, and so, while efficacious as drugs are much more likely to produce symptoms of poisoning.

The two substances, *para*-amidophenol and phenetidin being both excreted in the urine, chemical examination will show whether they appear rapidly or slowly, and so whether the original drug is stable or unstable in the organism. The urine may be examined every few hours after the administration of the drug in the following way (*v.* Jaksch and Garrod, *Clinical Diagnosis*)—

1. *For para-amidophenol.*—Boil the urine with one quarter of its bulk of strong HCl, and when cool add a few c.c. of a 3 per cent. phenol solution. Add a few drops of chromic acid solution. A red colour changing to blue on addition of NH_3 shows the presence of *para*-amidophenol.

2. *For phenetidin.*—Add 2 drops of HCl and 2 drops of a 1 per cent. solution of sodium nitrite. The latter will probably be unnecessary if the urine has been standing in a warm place for some hours, as sufficient nitrite will have been formed by bacterial action. Divide the specimen into two parts and add to one α-naphthol in a little sodium hydroxide. A red colour changing to violet on acidification with HCl will show presence of phenetidin, the depth of the tint being roughly proportionate to the amount present. To the other part add a few drops of phenol solution which will give a yellow colour in alkaline solutions and a rose-red on acidification.

(a) **Stable Substances.**—One of the hydrogen atoms in phenetidin may be replaced by a number of radicles giving compounds of the general formulæ—



where R stands for the substituting group—

Triphenin is proponyl phenetidin.
Dose: 8–15 gr. (0·5–1 gm.).

Salophen is salicyl phenetidin.
Dose: 10–30 gr. (0·6–2 gm.).

Amygdophenin is mandelic acid phenetidin.
Dose: 8–15 gr. (0·5–1 gm.).

Apolysin is said to be a citric acid phenetidin.
Dose: 8–30 gr. (0·5–2 gm.).

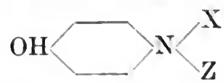
Phenosal is salicylacetic acid phenetidin.
Dose: 8 gr. (0·5 gm.).

Malakin is a salicylic aldehyde compound.
Dose: 10–30 gr. (0·8–2 gm.).

Eupyrin is a vanillin derivative.
Dose: 15–30 gr. (1–2 gm.).

All these substances are more or less insoluble in water and are feeble antipyretics. The salicyl compounds owe most of their action to that group, and have been given in acute rheumatism. Apolysin in acid media is more easily broken up and produces the toxic hydrochloride in the stomach. Malakin acts principally as a salicyl derivative and may cause gastric irritation. Eupyrin is hardly toxic, and has no analgesic action.

A rather different set of compounds is that in which both the hydrogen atoms in *para*-amidophenol are substituted, thus—



where X and Z stand for two different radicles *neurodin* and *thermodin* are substances of this class. Dose, 5–15 gr. (0·3–1 gm.). They are very feeble in action, the former is mainly analgesic and the latter antipyretic.

(b) **Unstable Substances.**—*Phenacetin* (acetyl phenetidin)—

is the best known and most widely used of this group. Although insoluble it has a considerable antipyretic action and is of still more value as an analgesic. It is not so toxic as acetanilide, which it closely resembles in its general pharmacological action, but is slower in taking effect. It is usually given in tablets. Dose, 5–15 gr. (0·3 gm.).

Lactophenin (lactyl phenetidin) is more soluble than phenacetin, and has a more marked hypnotic action. The dose is 5–15 gr. (0·3–1 gm.) and as much as 6 gm. have been given in one day. It is, however, liable to decomposition in the stomach with formation of phenetidin hydrochloride. Large doses, also, when continued over several weeks, appear to irritate the gastric and duodenal mucous membrane, and a certain number of cases of jaundice have been reported after its use. With smaller doses this condition is less liable to occur. It has been produced experimentally in rabbits. Although an unpleasant complication, it always clears up when the drug is discontinued.

Citrophenin is a substance of somewhat uncertain toxicity, and is variously regarded as a compound of citric acid with three molecules of phenetidin, or as a simple citrate. The dose is 8 gr. (0·5 gm.). It produces much sweating, and not a few cases of poisoning by comparatively small doses (1 gm.) have been recorded. The collapse which ensues is accompanied by extreme cyanosis. It has been recommended in whooping cough (2–3 gr. for every year of age), but it appears to have no advantages over phenacetin, than which, according to some authors, it is twice as toxic.

Phenocoll (glycocol phenetidin) and *cryophin* (methyl glycocol phenetidin) are similar substances, being soluble, rapidly absorbed and rapidly excreted. Their action is therefore transitory, and toxic symptoms are not uncommon. The dose is 8–15 gr. (0·5–1 gm.).

The three remaining substances in this group are rendered soluble by combining them in the form of salts. *Malarin* is a citric acid salt of methylbenzilidene phenetidin. It is in bitter yellowish crystals, and is markedly toxic. Dose, 5 gr. (0·3 gm.). *Pyrantin* is the sodium salt of the succinic acid compound of phenetidin (succinyl phenetidin). It has a sweetish taste, and is a more powerful protoplasmic poison than phenacetin. The dose is 15–45 gr. (1–3 gm.). It does not apparently destroy the red blood cells, but it has little effect on the thermotaxic centre and is an unreliable drug. *Phesin* is the sodium salt of sulphonic acid phenacetin, and is a light brown powder with a saltish taste. The entrance of the sulphonic acid radicle usually produces an increase in the solubility of an organic compound, but it is accompanied by weakening of the pharmacological action. Thus, though it would appear a less stable combination, owing to its solubility, it is very feeble in its effects. The dose is 15–30 gr. (1–2 gm.).

3. **The Phenylhydrazine Group.** — Phenylhydrazine is well known in the physiological laboratory, owing to the compounds it forms with sugars by which they are microscopically distinguished from each other. Its formula is—

It is powerfully toxic and its action in the body resembles that of aniline; in fatal cases death takes place from cerebral paralysis and convulsions. It gives rise to methæmoglobin in the blood and is a general protoplasmic poison.

Various attempts have been made to reduce the toxicity of phenylhydrazine while conserving its antipyretic action. The replacement of the hydrogen in the NH_2 group reduces the toxicity; the resulting compounds belong to the group called "hydrazones."

Lævulinic acid introduced in this manner gives a compound called *antithermin*. It is a gastric irritant and too toxic for practical purposes, though a powerful antipyretic. *Pyrodin* or hydracetin stands in the same relation to phenylhydrazine as acetanilide does to aniline, that is to say, a hydrogen atom of the NH_2 group is here replaced by acetyl—$C_6H_5.NH.NH.COCH_3$. But the toxicity is not sufficiently reduced for this substance to be practically useful.

In the compound known as *orthin* the ring is attacked, two of its hydrogen atoms being replaced by hydroxyl (OH) and carboxyl (COOH) respectively. The nitrogen groups are left untouched. Its action is, however, uncertain, and its toxicity high.

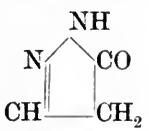
Maretin is a substance in which both methods of replacement have been tried. One of the ring hydrogens is replaced by methyl (CH_3) and one of the NH_2 hydrogens by $CONH_2$ (the carbamic acid radicle). Its formula, therefore, is $C_6H_4CH_3.NH.NH.CONH_2.(1:3)$. It is sparingly soluble and tasteless. The dose is 3–8 gr. (0·2–0·5 gm.). This drug is less toxic than the phenylhydrazine derivatives previously mentioned, and in doses not greater than 0·5 gm. is entirely eliminated in twenty-four hours. It is, however, a blood poison and may cause jaundice. If taken for several consecutive days anæmia, cyanosis and collapse may occur, and it is a gastro-intestinal irritant. The antipyretic action is liable to be accompanied by profuse and exhausting perspiration.

Cryogenin is a similar substance, two carbamic acid radicles being introduced instead of one;

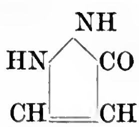
the second takes the place of the methyl group in maretin. It is not sufficiently soluble to be given in water, and has a pleasant taste resembling almonds. The dose is 3–15 gr. (0·2–1 gm.). Elimination is slow. It has little or no analgesic action and is not a powerful antipyretic. Its continued use may cause anæmia, and in some cases varying degrees of collapse have occurred. It does not seem, therefore, to be any improvement on the older antipyretics.

4. The Pyrazolon Group. — Chemically this cannot perhaps be considered a separate group, as its members are derived, though rather remotely, from phenyl hydrazine. Their characteristics are, however, very different from those of that substance, and their structure shows a considerable amount of modification; so that it is convenient to place them together under a somewhat more nearly connected origin.

Pyrazolon and its isomer *iso*-pyrazolon, have the following structure—

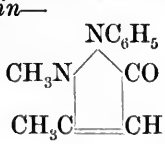


Pyrazolon



iso-Pyrazolon

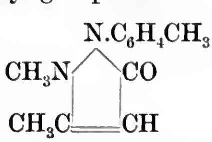
Substitution of three hydrogen atoms by methyl and phenyl results in the production of an antipyretic drug well known as *phenazone* or *antipyrin*—



[dimethyl-phenyl-Pyrazolon]

This substance, which is soluble, is excreted in the urine, partly unchanged and partly as a glycuronic acid compound. Its pharmacological properties do not differ from those of the other well-known antipyretics, acetanilide and phenacetin, and it stands in point of toxicity midway between the two. It was formerly given in large and frequent doses, but at present doses of 15 gr. are rarely exceeded. Its main practical convenience lies in its solubility.

Tolypyrin differs from antipyrin in having one more methyl group—



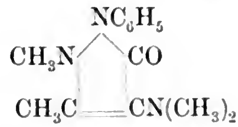
It is insoluble, a less powerful analgesic and a gastric irritant. The dose is the same as that of antipyrin.

Tolysal and *Salipyrin* are compounds of salicylic acid and antipyrin. They are broken down into their constituents by dilute hydrochloric acid, so that their effect is simply that of a mixture of these drugs.

Tussol is a similar compound with mandelic acid. It has been used in whooping cough, but presents no advantages over antipyrin in the treatment of this disease.

Anilopyrin is a compound of acetanilide and antipyrin; if necessary these drugs may easily be prescribed together in appropriate doses with exactly the same effect.

Pyramidon is dimethyl-amidoantipyrin—



It is soluble in water, the solutions being alkaline and possessing a very slight bitter taste. The dose is 3–8 gr. (0·2–0·5 gm.), 5 gr. being usually effective. It is said to increase nitrogenous metabolism, and experimentally it does not give rise to fatty changes in the organs or destruction of red blood cells in toxic doses. One death from pyramidon has been reported, and occasionally the usual toxic symptoms observed with the other antipyretic drugs have been observed. It is, however, on the whole, a very safe drug and a very efficient analgesic. Five grains usually remove headache or neuralgic pains, to a great extent, in half to three-quarters of an hour. Combined with salicylates it is useful in stopping the neuralgic pains usually attributed to rheumatism.

Pyramidon is excreted in the urine partly unchanged, partly combined with glycuronic acid and partly as uramino antipyrin. On standing, a red colouring matter develops in the urine, called rubazonic acid.

Melubrin is another antipyrin derivative, in which the hydrogen atom is not replaced by a dimethyl-amido group, but by the sodium compound amido-methane sulphonic acid—

$$-N<^{H}_{CH_2.SO_2.NaO}$$

It is soluble and nearly tasteless. The dose recommended varies from 7½–30 gr. (0·5–2 gm.). It is said to be a mild antipyretic, and to be useful as a substitute for salicylates in acute rheumatism. Its chemical structure, containing as it does the sulphonic acid group, seems to indicate that it is not very toxic, but it is more than doubtful if this decrease in toxicity is likely to be accompanied by vigorous therapeutic action (compare *Cosaprin*).

Preparations

Acetanilidum (B.P., U.S.P.). Antifebrin. Colourless crystals, insoluble in water, soluble in alcohol, ether and chloroform.

Dose: 2–5 gr. (12–30 cg.). Larger doses are often prescribed, up to 10 gr.

Pulvis Acetanilidi Co. (U.S.P.). Acetanilide 7, caffeine 1, sodium bicarbonate 2.

Dose: 8 gr. (0.5 gm.).

Phenacetinum (B.P.), *Acetphenetidinum* (U.S.P.) Colourless, insoluble crystals.

Dose: 5–15 gr. (3–10 dg.).

Phenazonum (B.P.), *Antipyrina* (U.S.P.). Colourless, bitter-tasting crystals, soluble in water, alcohol and chloroform.

Dose: 5–15 gr. (3–10 dg.).

Antipyrinæ Salicylas (B.P.C.). "Salipyrin." Colourless insoluble crystals.

Dose: 10–30 gr. (6–20 dg.).

Phenocolli Hydrochloridum (B.P.C.). Colourless crystals with a sharp, bitter taste. Soluble in water (1 in 16) and alcohol.

Dose: 7–15 gr. (0·5–1 gm.).

Phenylurethanum (B.P.C.). Colourless crystals with slight, burning, aromatic taste. Sparingly soluble in water. Soluble in dilute spirits.

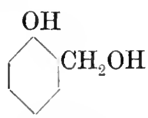
Dose: 1–8 gr. (6–50 cg.).

J. M. F.-B.

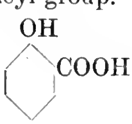
THE SALICYL AND BENZOYL COMPOUNDS

Salicyl and its Derivatives

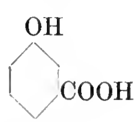
In the bark of various species of willow (*salix*) and poplar (*populus*) a glucoside occurs which has been named salicin. On hydrolysis it yields glucose and an alcohol, saligenin, the formula for which is



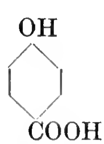
The corresponding acid is salicylic acid, or *ortho*-oxybenzoic acid, which can be prepared from oil of wintergreen, derived from *Gaultheria procumbens*, but is now usually manufactured synthetically. Three oxybenzoic acids are known, differing in the relative positions of their side chains, namely *ortho*, *meta*, and *para* oxybenzoic acid, but it is remarkable that only the first of these shows the well-known physiological effects of the salicyl group.



Ortho



Meta



Para

The other two have a very feeble antiseptic and antifermentative action, and no specific effect in acute rheumatism. Salicylic acid, with its two side chains, offers a large field to the pharmacological chemist, and many derivatives have been prepared by substituting various groups in one or other or in both; the action of these bodies, however, in the animal organism depends essentially on the negative salicyl ion, C_6H_5.OH.CO, so that it will be convenient first to describe the pharmacological action of salicylic acid, and then to compare the numerous derivatives with the parent substance.

1. **Salicylic acid** has a powerful antiseptic action, and acts as a protoplasmic poison on the lower organisms. It also checks fermentation, but owing to its non-volatile nature it has not the same penetrative power as corresponding solutions of phenol. When taken into the animal body it is rapidly absorbed, it may produce some gastric irritation, and is caustic when taken in solid form. Its more important effects are shown on the nervous system, through which it produces (1) cutaneous vaso-dilatation, (2) profuse perspiration, (3) slight quickening of the respiration, (4) a transient rise of blood pressure. Larger doses produce symptoms ("salicylism") similar in some respects to those of quinine, namely, buzzing in the head and deafness, dimness of vision, erythematous and other rashes, epistaxis and other hæmorrhages, and delirium. The sensory and cutaneous phenomena have been ascribed to vascular engorgement; they usually pass off completely when the drug is discontinued. Poisonous doses produce profound depression of the medullary centres, but there are no convulsions, except such as are occasionally set up by asphyxia.

The heart is only slightly accelerated by small doses, the skeletal muscles are unaffected, the liver is said to be slightly stimulated and the flow of bile increased.

Salicylic acid stimulates nitrogenous metabolism, both nitrogen and sulphur excretion being augmented, especially the former. There is marked increase in the uric acid eliminated, which may be due to augmented katabolism.

Salicylic acid is excreted by the kidneys. It circulates in the blood as an alkaline salt and is combined in the kidneys with glycocoll (aminoacetic acid, CH_2NH_2COOH) to form an inert substance, salicyluric acid. A little passes unchanged, and a little pyrocatechin, $C_6H_4(OH)_2$, is also formed, giving the urine a greenish tinge. Large doses are said to cause renal irritation with albuminuria and hæmaturia, like phenol and other coal-tar derivatives.

The therapeutic value of salicylic acid may in part be inferred from its pharmacology. Externally it may be used as an antiseptic, but it has now been replaced by other substances in surgical practice. A 3 per cent.

powder in talc or some other convenient medium is often used for dusting sweating feet, or in phthisis; a drachm of salicylic acid in an ounce of flexile collodion is a useful solvent for corns, the antiseptic action may share in the extermination of the corn. The tincture of cannabis indica often added to this solution is quite unnecessary. The addition of salicylic acid to beer, preserves, etc., in order to enhance their keeping qualities may be harmless in itself, but is very inadvisable, as it allows an inferior or rotten article to be made equally salable as a sound one.

Internally salicylic acid has been employed as an intestinal antiseptic, but its value is doubtful; at any rate its administration does not alter the amount of indican in the urine. Owing to its diaphoretic action it is able to reduce the temperature in fever, and it has a mild analgesic action. It is not often employed thus in this country. It is of little practical value as a cholagogue.

The main and most valuable property of salicylic acid and its sodium salt cannot, however, be deduced from an experimental investigation of its pharmacological action. Shortly after its introduction as an antipyretic in 1876, it was discovered to have a "specific" effect in acute rheumatism. In this disease it should be given from the beginning of the attack in full doses, well diluted with water, 20 gr. (1·3 gm.) every two or three hours until the symptoms are relieved or signs of intoxication begin. After twenty-four hours the dose may be reduced, but for two or three weeks 15 gr. should be administered thrice daily. The sodium salt is a more soluble and convenient preparation than the acid, and in order to diminish the danger of acidosis should be combined with an equal weight of sodium bicarbonate. It has probably little effect on the cardiac complications of acute rheumatism, but owing to the fact that severe cases are cut short and the patients survive, there may be an apparent increase in the percentage of those who subsequently suffer from chronic endocarditis. It is thought by some to diminish the liability to pericarditis, and has also been found of value in other conditions associated with serous effusions. There is no advantage in giving sodium salicylate intravenously, but 2 or 3 gr. (0·2 gm.) may be injected locally in 15 min. (1 c.c.) of water, for the temporary relief of a very painful joint. A 2 per cent. solution of sodium salicylate has also been applied to painful joints, and the salicyl ion driven in by the kathodic pole of a galvanic battery, but this is an unnecessary procedure for the most part, as true acute rheumatism responds so well to the drug when administered internally.

In rheumatoid arthritis, chronic rheumatic pains or the so-called rheumatic myositis and fibrositis, salicylic acid acts far less well, and is often practically valueless. In these cases, as in some neuralgias, the method of ionisation may be tried and is sometimes successful in reducing the pain, but much less so in rheumatoid and osteo-arthritis than in the affections of muscles and fasciæ. A large electrode soaked in the 2 or 3 per cent. solution of sodium salicylate is placed over the affected area and a current of from 10 to 30 ma. (as strong as can be tolerated by the patient) is passed for half an hour or longer. The salicyl, being an anion, is applied by the kathode. In other cases the limb may be placed in a bath of the solution, through which the current is passed, the positive electrode being applied higher up on the same limb.

Salicylate of sodium is often added to mixtures intended to relieve the paroxysms of gout, but its value is very doubtful. The fact that it increases the excretion of uric acid is no proof that it will act beneficially, as the effect is due to increased destruction of cells and not to improved elimination of waste products.[1] It is also given in the lightning pains of tabes, sometimes with benefit, and in diabetes, migraine, and some skin diseases, such as psoriasis in its early and spreading stages. In all these conditions the action of the drug is inconstant, though it is worthy of trial.

It should be given cautiously if there is evidence of renal inflammation.

Recently the interesting suggestion has been made (H. E. Waller) that salicylates may act by influencing thyreoid activity. It has been pointed out that the effects of salicylic acid compounds may be compared in some respects to those attributed to thyreoid inadequacy, and that some cases of Graves' disease and thyreoiditis may be benefited by their administration. Further clinical experience is required before this can be established, and in view of the slight toxicity of salicyl compounds, no harm is likely to result from their experimental exhibition in these cases.

The Metallic Salts of Salicylic Acid.—*Sodium salicylate* may be regarded as precisely similar in its internal action to salicylic acid; externally it is not usually employed, but it has some antiseptic power.

It was at one time thought that sodium salicylate prepared from oil of wintergreen was less toxic than the manufactured synthetic salt, but this appears to have been due to impurities in the latter, which can be avoided by improved methods of production. The impurities are stated to be mainly cresotinic acids.

[1] This may also be due to a diminished decomposition of uric acid precursors.—Walker Hall.

At present nearly all the sodium salicylate on the market is prepared synthetically, and is very much cheaper than the so-called "natural" salt.

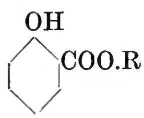
Lithium salicylate was introduced owing to the supposed value of both its constituents in gout, but as it is now known that neither has any therapeutic value in this condition its use had better be discontinued.

Bismuth salicylate is an amorphous insoluble powder, chiefly used as a gastro-intestinal disinfectant. Its action is mainly due to the bismuth, and the dose is 5 to 20 gr. (0·3–1·2 gm.). It is useful in the diarrhœic diseases of infants.

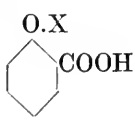
3. **Organic Salicyl Compounds.**—The remaining compounds are most conveniently considered under two headings according as they are intended for internal or external administration. Chemically they all fall into one of four groups, which can easily be grasped by reference to the structure of salicylic acid.

In the first group will come those bodies which are related to, but not strictly derivatives of, salicylic acid; these are salicin and salinigrin, the glucosides, saligenin, the corresponding alcohol, and the cresotinic acids which are homologous methyl derivatives.

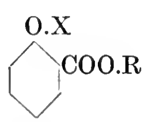
In the second group will come those bodies in which the hydrogen of the acid (COOH) group is replaced by an organic radicle, and which are thus esters of salicylic acid, having the general formula—



In the third group will come those bodies in which the hydrogen of the hydroxyl (OH) group is similarly replaced—



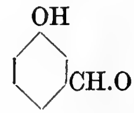
In the fourth group will come those bodies in which both these hydrogen atoms are replaced, and which consequently will have the general formula—



A. Internal Remedies

Group I.—*Salicin* is hydrolysed in the body into glucose and saligenin, the latter being then oxidised to salicylic acid. The yield of salicylic acid is less than half the weight of the original dose of salicin, so that adequate doses must be about double those of sodium salicylate. Thirty to sixty grains may be given every two hours in acute rheumatism, well diluted. It is soluble in warm water and less likely to disturb the stomach than sodium salicylate. Some authorities state that it is entirely decomposed in the body, others that a considerable portion is excreted unchanged.

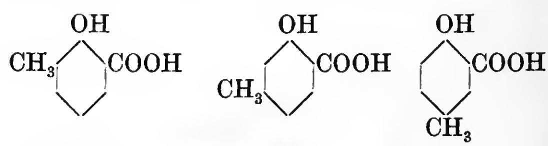
Salinigrin is a glucoside obtained from Salix Nigra or black willow, and is a soluble body yielding on hydrolysis glucose and *meta*-oxybenzaldehyde.



It has been employed as an urinary antiseptic in gonorrhœa, and to relieve various pelvic pains. The aldehyde is doubtless oxidised in the body to the corresponding acid, which is known to be less efficacious than salicylic acid both in acute rheumatism and as an antiseptic.

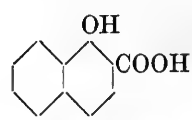
Saligenin, the corresponding alcohol to salicylic acid, is a white powder easily soluble in warm water. It is oxidised in the body to its acid, and may be given in doses of 10 gr. two-hourly. Its action naturally does not differ from that of sodium salicylate, but it is less irritant to the mucous membrane.

There are three isomeric *cresotinic acids*, which are all derived from salicylic acid and differ only in the position of the methyl (CH_3) group—



Ortho Meta Para

These act in the same way as salicylic acid, the *ortho* compound being the most powerful; the relative efficacy of the other two has been variously stated by different observers, but as none of them are in any way superior to salicylic acid itself, the question is of no practical therapeutic importance. The oxynaphthoic acids

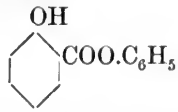


α-naphthol carboxylic acid

of which there are fourteen isomers, act similarly to salicylic acid, but are too toxic for use in medicine.

Group II.—*Salol* is the oldest and in some ways the best-known member of this group.

It is the carbolic acid ester of salicylic acid, and has the formula—



In the intestine it is split up into salicylic acid and phenol, and large doses may give rise to carboluria and other symptoms of phenol poisoning. It is thus unsuitable for use in rheumatic conditions, as enough salicylic acid cannot safely be administered by its means. It has, however, been somewhat largely used as an intestinal antiseptic, though it fails to reduce the amount of indican in the urine, and clinically the evidence of its efficiency is not particularly strong. It has also been employed as a urinary antiseptic in gonorrhœa, and is a common constituent of mouth-washes. It is insoluble in water, and when administered for a long period has been known to accumulate in hard masses in the bowel, causing obstruction.

Diaspirin is the succinic acid ester of salicylic acid, and is insoluble in water. The dose is stated to be 8 to 15 gr. (0·5–1 gm.), but maximum doses are necessary to produce diaphoresis.

Novaspirin is the methylene citric acid ester, is almost insoluble in water, and hardly produces any sweating. The dose is 8 to 15 gr. (0·5–1 gm.).

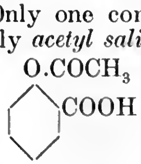
Rheumatin is the salicyl quinine ester, and so contains two salicyl groups and one quinine group in its molecule. It is insoluble in water. The dose is 15 gr. (1 gm.).

Salacetol is the acetol ($OHCH_2COCH_3$) ester. It is insoluble. The dose is 30 to 45 gr. (2–3 gm.) daily.

Salimenthol, the menthol ester, is an oily liquid, not miscible with water, and must be given in capsules. The maximal dose is 4 gr. (0·25 gm.) several times daily.

Salophen is an ester of acetyl-*para*-aminophenol ($OH.C_6H_4NHCOCH_3$) and salicylic acid. It is insoluble, and the dose is 8 to 15 gr. (0·5–1 gr.). It is broken up into its constituents in the small intestine.

GROUP III.—Only one compound occurs in this group, namely *acetyl salicylic acid*—



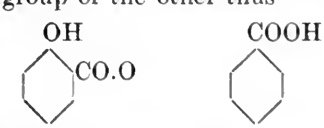
which is also known by various trade names—aspirin, acetosal, aletoidin, saletin, xaxa, etc. It is only slightly soluble in water, and is usually stated to pass through the stomach unchanged, and to be decomposed in the small intestine, yielding sodium salicylate, which is absorbed as such. It seems probable, however, that a very small proportion may be broken up in the acid stomach contents, liberating free salicylic acid, which passes rapidly into the duodenum and starts the physiological action. The dosage is the same as that of sodium salicylate, but owing to its poor solubility it must be prescribed in cachets or powders or else suspended in mucilage. Ten grains of the powdered acid with 90 min. of tragacanth mucilage may be ordered in ½ oz. of water (Martindale), but owing to the instability of the drug, a gradual decomposition takes place in all solutions, especially in hot weather. There could, however, be no objection to dispensing small quantities in solution if necessary, provided the medium were neutral and no other drug were added to the mixture. The action of acetyl salicylic acid is that of the salicylic acid radicle; but many think that clinically it has a more general analgesic action, and is more useful in painful affections, other than acute rheumatism, than is sodium salicylate. It has the obvious disadvantage that it cannot be prescribed with alkalies (which decompose it), and this may add to the chances of acidosis in rheumatic cases. In a certain number of persons (though probably not many) small doses (5 gr.) produce extensive œdema of the face and urticaria—an alarming but usually transitory condition. After absorption it may, of course, produce exactly the same toxic symptoms as any other salicyl compound.

GROUP IV.—*Aspirophen* is chemically aminophenacetin combined with acetyl salicylic acid. It is not very soluble in cold water; the maximum dose is 15 gr. (1 gm.).

Benzosalin is the methyl ester of benzoyl salicylic acid, and is insoluble; the dose is 10 to 25 gr. (0·6–1·6 gm.).

Methyl Rhodin or *Methyl Aspirin* is the methyl ester of acetyl salicylic acid; it is insoluble and given in the same doses as sodium salicylate.

Diplosal is the salicyl ester of salicylic acid and might chemically be considered to belong to either the second or third group and in a sense belongs to the fourth. The alcoholic radical in one salicylic acid molecule is combined with the carboxyl group of the other thus—



It is insoluble in water, and decomposed by dilute alkalies. The dose is 15 to 30 gr. (1–2 gm.) thrice daily. It is quite obvious that as the efficacy of all these drugs depends on the same factor, there can be no marked superiority in one over the other—provided an equal dosage of the salicyl radicle is given—at any rate as regards their curative action in acute rheumatism. The gastric disturbance which is sometimes set up by a soluble salicylate

may be avoided by giving an insoluble body, or the glucoside or saligenin. But after all, sodium salicylate is well tolerated by most people, even in large doses, when properly diluted and given with an alkali, and the claims of the newer preparations to superiority have little or no foundation in fact. An interesting series of observations carried out by Hanzlik showed that the mean dose producing toxic symptoms (tinnitus, etc.) in adult males for several salicyl preparations was as follows—

Synthetic sodium salicylate 180 gr.
Natural sodium salicylate 200 gr.
Methyl salicylate 120 min.
Acetylsalicylic acid 165 gr.
Salicyl-salicylic acid 100 gr.

Idiosyncrasy to salicyl did not appear to be influenced by age, sex, race or the nature of the disease, and the results show that toxic symptoms appear after much the same dose of sodium salicylate or acetyl salicylic acid, though the latter has a slightly smaller average dose. Methyl salicylate is not generally suitable for internal administration.

B. External Remedies

These are all esters of salicylic acid, and thus belong to the second of the chemical groups described above.

Methyl Salicylate, $OH.C_6H_5COOCH_3$, is the main constituent of natural oil of wintergreen (from *Gaultheria procumbens*) and oil of sweet birch (from *Betula lenta*), and is an oily substance only slightly miscible with water, but miscible in all proportions with alcohol, ether, chloroform and oils. It has a burning aromatic taste, and though efficacious therapeutically should not be given internally, as it is very apt to upset the stomach. It is largely used as a local application to painful joints and muscles; absorption occurs through the skin and salicyluric acid appears in the urine. It may be applied either pure or diluted, and the area covered with flannel or gutta-percha tissue. It is somewhat irritant, however, and care must be taken not to produce too strong a local reaction. The synthetic oil is said to be less irritant than the natural one. Its strong pungent odour is disagreeable to some persons.

Glycosal is the monoglycerin ester, a white, crystalline powder, and resembles methyl salicylate in being insoluble in water, but readily so in alcohol or glycerin. A 10 per cent. ointment in lanolin or a 20 per cent. paint in spirit or glycerin may be used. It is somewhat irritant.

Mesotan is the methoxy-methyl (CH_2OCH_3) ester, and is a liquid miscible with oil, chloroform, alcohol, etc., but not with water. Its main advantage is that it has hardly any odour, and its disadvantage is that it readily decomposes with the formation of formaldehyde, HC.H.O, an irritant substance which is liable to set up severe dermatitis. It may be applied with an equal part of olive oil as a paint and lightly covered with a bandage, but an impervious covering like gutta-percha should be avoided. A convenient application is methoxy-methyl salicylate 2, ichthyol 2, olive oil 6 parts.

Salen is a mixture of two crystalline bodies, the methyl and ethyl glycolic acid esters, which liquefy when rubbed up together. It is odourless and resembles mesotan in its solubilities. A 33·3 per cent. ointment is called Salenal.

Sainol is a 25 per cent. ointment of salimenthol.

Salit is the borneol ester. It is an oily liquid, and is best applied with an equal part of olive oil. One half to one drachm may be painted on the skin daily and covered with wool or flannel. To avoid dermatitis the skin should be thoroughly washed with soap and water and alcohol before the application.

Salocreol is a creosote compound, and is a brown oily fluid with a disagreeable odour. It is applied without dilution.

Spirosal, the glycolic acid ($OH.CH_2COOH$) ester, is an oily liquid miscible with the ordinary solvents, but not very soluble in olive oil (1 : 15) or water (1 : 110). It is applied with an equal part of spirit, and resembles mesotan in possessing no odour. It is also said to be less irritant. One half to one teaspoonful may be applied once or twice a day.

The newer preparations have no marked advantage over oil of wintergreen, except in some cases the absence of odour.

Salicylic acid itself, in the form of a 15 per cent. ointment in lanolin, is well absorbed, and probably of equal value to most of the synthetic esters. The rubefacient action of the more irritant oils is, however, an advantage as producing at once free absorption of the drug and counter-irritation over the diseased area.

Preparations

Acidum Salicylicum (B.P., U.S.P.). 5–20 gr. (3–12 dg.).
Unguentum Acidi Salicylici (B.P.). 2 per cent.
Salicinum (B.P., U.S.P.). 5–20 gr. (3–12 dg.).
Acidum Acetylsalicylicum (B.P.). 5–15 gr. (3–10 dg.).
Salol (B.P.), Phenylis Salicylas (U.S.P.). 5–20 gr. (3–12 dg.).
Sodii Salicylas (B.P., U.S.P.). 10–30 gr. (6–20 dg.).
Methyl Salicylas (B.P., U.S.P.). 5–15 min. (3–10 dl.).
Oleum Gaultheriæ (B.P., U.S.P.). 5–15 min. (3–10 dl.).
Spiritus Gaultheriæ (U.S.P.). 15 min. (1 ml.) as a flavouring agent.

Bismuthi Salicylas (B.P., U.S.P.). 5–20 gr. (3–12 dg.).

B.P.C. Preparations.

Collodium Salicylicum. 1 of Salicylic Acid in 8.

Collodium Salicylicum Co. 12 per cent. Salicylic Acid contains also Indian hemp.

Emplastrum Salicylicum Elasticum. 1 of Salicylic Acid in 10.

Emplastrum Salicylicum Co. 20 per cent. Salicylic Acid.

Emplastrum Salicylicum Co. Fortius. 40 per cent. Salicylic Acid. Both contain also Indian hemp.

The above are intended as applications for corns. The following also contain Salicylic Acid. The Gossypium 4 per cent., Gossypium Forte 10 per cent., Linteum 4 per cent., Paragenum 10 per cent., Sevum 2 per cent., are intended for surgical dressings.

Pulvis Acidi Salicylici Co. 3 per cent. with boric acid and French chalk is intended for sweating surfaces.

Granulæ Salicini (effervescent). 60–120 gr. (4–8 gm.).

Tablellæ Salicini. Contain 5 gr. Salicin each.

Liquor Salolis Æthereus. Is used as a coating for pills to prevent disintegration in the stomach.

Liquor Salolis Co. 2.5 per cent. Contains also thymol, anise, peppermint, gluside and alcohol. A few drops in a wine-glassful of water makes an antiseptic mouth-wash.

Tablellæ Salolis. Contain 5 gr. Salol each.

Granulæ Sodii Salicylatis (effervescent). 1 in 12½. 60–180 gr. (4–12 gm.).

Tablellæ Acidi Acetyl-salicylici. Contain 5 gr. each.

Linimentum Methylis Salicylatis. Contains menthol 5, oil of eucalyptus 10, essential oil of camphor 25, methyl salicylate to 100. It is miscible with spirit and oil.

Linimentum Methylis Salicylatis Co. Contains no oil of eucalyptus, but instead chloral hydrate 5, and extract of Indian hemp 0·5.

The paste, ointment and compound ointment contain 50 per cent., the dilute ointment and dilute compound ointment contain 25 per cent. of methyl salicylate.

Extractum Salicis Nigræ Liquidum. 1 in 1. *Dose:* 15–60 min. (1–4 ml.).

U.S.P. Preparations.

In addition to salicylic acid, sodium salicylate, salicin, phenyl salicylate (salol), methyl salicylate, oil and spirit of gaultheria and bismuth salicylate, the following are official in the U.S.P.—

Lithii Salicylas. 15 gr. (1 gm.).

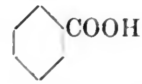
Ammonii Salicylas. 4 gr. (25 cg.).

Strontii Salicylas. 15 gr. (1 gm.). They are all three unnecessary compounds.

Oleum Betulæ. 15 min. (1 ml.).

Benzoic Acid and its Derivatives

1. **Benzoic Acid,** which is the corresponding



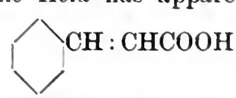
acid to phenol, may be obtained from certain balsams or resinous substances occurring in trees or shrubs of the families of the Leguminosæ, Saxafrageæ and Styraceæ in tropical and subtropical zones. It may also be manufactured from toluene, $C_6H_5.CH_3$, and other aromatic bodies.

The acid itself is a light, feathery crystalline body soluble only in 450 parts of cold water. Its physiological action closely resembles that of salicylic acid, though it is not so powerful. It is but slightly irritant to the mucous membrane of the stomach and intestine, has marked antiseptic properties, and a mild action in acute rheumatism, both reducing the temperature and modifying the arthritis. It does not produce sweating, but slight buzzing in the ears has been noticed. It produces a polymorphonuclear leucocytosis and increases nitrogenous metabolism. The indican in the urine is diminished, so that it probably has some action in diminishing intestinal putrefaction. In the kidneys it is synthesised, as is salicylic acid, with glycocoll, CH_2NH_2COOH, producing hippuric acid; but some is excreted unchanged. It thus acts as a urinary antiseptic. Some glycuronic acid is also apparently formed, as the urine may reduce Fehling's solution.

Therapeutic Applications.—These are somewhat limited, as most of the pharmacological properties of benzoic acid are possessed in a higher degree by other substances. Ammonium benzoate is, however, a common ingredient in mixtures intended to disinfect the bladder in cystitis and gonorrhœa, and it may also be used as an intestinal antiseptic.

Guaiacol benzoate and β-naphthol benzoate depend on their content in guaiacol and β-naphthol for their main pharmacological action.

2. *Cinnamic Acid* has apparently a similar



physiological action. Its most marked properties are the power of increasing the polymorphonuclear leucocytes and the nitrogenous excretion (especially uric acid). The power, however, is not constantly observed where the drug is given by the mouth to human beings. The sodium salt was introduced as a remedy for phthisis under the name of *Hetol*, but the results were not striking, and it has practically been abandoned.

3. The *Balsams* are mixtures of resin, volatile oils and various aromatic bodies, of which the principal are benzoic and cinnamic acids, cinnamein (benzylic benzoate and cinnamate) and styracin (the cinnamic ester of cinnamyl alcohol).

Benzoin contains the two acids in varying proportions, and is derived from several *Styraceæ*. *Styrax*, from *Liquidambar orientalis*, contains cinnamic acid and styracin. *Balsam of Peru* from *Myroxylon pereiræ* contains cinnamein, *Balsam of Tolu* from *M. Toluifera* contains more benzoic and cinnamic acids and less cinnamein.

Therapeutic Uses.—The balsams are used internally as ingredients in cough mixtures, as they appear to stimulate the secretion of mucus and to render it less tenacious. The syrup of Tolu which is commonly prescribed contains so little of the balsam that it is hardly more than a flavouring agent. The compound tincture of benzoin is well known as a stimulant expectorant and is generally added to boiling water (1 dr. in 1 pint) for inhalation or used with other aromatic oils on a respirator.

Externally the balsams are now practically only used as parasiticides. The balsam of Peru, in the form of the Unguentum, or Styrax (with an equal part of olive oil and white wax), may be applied in scabies or pediculosis, and though more expensive are pleasanter preparations than sulphur ointment. When large quantities of the balsams are absorbed, resinous bodies may appear in the urine which give a precipitate with acids; this may be distinguished from albumen by its solubility in alcohol. A few undoubted cases of albuminuria have, however, occurred (Allen), and some German authors report the occurrence of albumen, blood and tube casts in the urine after extensive applications of Balsam of Peru.

Preparations

Acidum Benzoicum (B.P., U.S.P.). 5–15 gr. (3–10 dg.).

Trochiscus Acidi Benzoici (B.P.). ½ gr. (3 cg.) in each.

Ammonii Benzoas (B.P., U.S.P.). 5–15 gr. (3–10 dg.).

Sodii Benzoas (B.P., U.S.P.). 5–30 gr. (3–20 dg.).

Lithii Benzoas (U.S.P.). 15 gr. (1 g.). Intended for administration in gout, but practically useless. It should be omitted.

Benzoinum (B.P., U.S.P.).

Tinctura Benzoini Composita (B.P., U.S.P.). Contains benzoin, storax, aloes and tolu balsam. ½–1 fl. dr. (2–4 ml.).

Tinctura Benzoini sine Aloe (B.P.C.). Used for inhalation. (1 part in 200 of water at 60° C.).

Tinctura Benzoini (U.S.P.). 20 per cent. 15 min. (1 ml.).

Tinctura Benzoini (B.P.C.). 10 per cent. ½–1 fl. dr. (2–4 ml.).

Adeps Benzoatus (B.P.). 3 per cent.

Sevum Benzoatum (B.P.). 3 per cent.

Lotio Benzoini (B.P.C.). 1 in 40 of Rose Water.

Lotio Benzoini Composita (B.P.C.), with quillaia tincture and Eau de Cologne. A cosmetic.

Nebula Benzoini Composita (B.P.C.), with soil of pine, eucalyptus, cassia, menthol and glycerin.

Nebula Benzoini Composita cum Cocaina et Quinina (B.P.C.), with cocaine hydrochloride, 0·75 per cent., camphor, quinine hydrobromide, and antipyrin.

Styrax Præparatus (B.P.), Styrax (U.S.P.).

Balsamum Tolutanum (B.P., U.S.P.). 5–15 gr. (3–10 dg.).

Syrupus Tolutanus (B.P., U.S.P.). ½–1 fl. dr. (2–4 ml.).

Tinctura Tolutana (B.P., U.S.P.). ½–1 fl. dr. (2–4 ml.).

Liquor Tolutanus (B.P.C.) is used to prepare—

Syrupus Rolutanus (B.P.C.). ½–1 fl. dr. (2–4 ml.).

Balsamum Peruvianum (B.P., U.S.P.). 5–15 min. (3–10 dl.).

Collodium Peruvianum (B.P.C.). 1 in 10.

Unguentum Peruvianum (B.P.C.). 1 in 10. Both for use as parasiticides.

J. M. F.-B.

PURGATIVES AND CHOLAGOGUES

Purgatives are substances which cause evacuation of the bowel. In the course of their action they render the fæces more fluid than normal, and, broadly speaking, the more potent the purgative the higher is the proportion of water in the dejecta. The term *hydragogue carthartic* is frequently used to denote the more powerful or *drastic* purgatives; while *eccoproctic*, *laxative* and *aperient* are terms descriptive of purgatives which have a milder action. A large number of substances will induce purgation, but many of these are not commonly used in therapeutics, because they have other undesirable effects on the organism. It is natural that substances which act almost exclusively on the alimentary canal should be preferred; and fortunately a number of such are at our disposal. Of these, again, substances which cause irritation in the stomach are also objectionable since, apart from the sensation of nausea they produce, they are liable to cause vomiting. The localisation of the effect to the alimentary canal is effected by the employment of substances which are either not absorbed, or absorbed with difficulty, after oral administration. And the limitation

of action to the terminal portion of the alimentary canal is accomplished by the use of substances which only become active after they have undergone some chemical alteration in the intestines, or which are insoluble except in the presence of bile.

The purgatives have been classified in a number of different ways, but none of these are entirely satisfactory. Classification on the basis of evacuating power, under the terms drastic, cathartic, laxative, etc., fails, because the effects of large and small doses of one and the same drug indicate that it belongs to two classes. Classification on the basis of the chemical nature of the purgative is unsatisfactory because in many instances we do not know enough about the chemical nature of the active principles; and in other instances the physical and chemical properties of purgatives do not appear to have any direct relationship to their pharmacological values.

The purgatives are best sub-divided into groups according to the method of their action.

1. Substances which induce purgation by virtue of their irritant properties, such as *senna, aloes, castor oil*, *jalap* and *calomel.*

2. Substances which cause evacuation of the bowel by increasing the water content of the intestines, such as *sodium sulphate.*

3. Substances which stimulate the neuromuscular mechanism of the alimentary canal, such as *physostigmine.*

The irritant purgatives may be further divided into (*a*) those which act for the most part upon the large intestine, and (*b*) those which act on both large and small intestines.

Group I.—The Action of Irritant Purgatives

The two prominent features of purgative action are: the increased rate of passage of material along the alimentary canal, and the high water content of the fæces. The former is indicated by the presence of partially digested material in the excreta, and is proved by measurement and comparison of the times taken for some harmless substance to pass through the body, (1) in normal circumstances, and (2) under the influence of purgatives. It has further been shown, by means of insoluble bismuth salts and X-rays, that some substances hardly affect the rate of transit in the small intestine, but have a pronounced effect in the large; others increase the rate in both large and small intestines.

The movements of the intestines are regulated by peripheral reflexes in the intramuscular and submucous nerve plexuses. Peristalsis is readily evoked by mechanical stimuli or mild irritants, such as hypertonic salt solution, applied to the mucous membrane. Purgatives by virtue of their irritant properties cause vigorous peristalsis. The increased force and frequency of peristaltic movements has been demonstrated by recording the rate of passage of an india-rubber balloon or other bolus down the intestine (Brandl, Tappeiner). The pull on a thread attached to the bolus gives a rough estimate of the force, and this has been found to be about three times as great as in a control experiment.

Those substances which act upon the small intestine thus hurry the contents into the colon, where nearly all purgatives have an irritant action. By a precisely similar mechanism usually powerful muscular movements are called forth. In animals X-ray methods have shown that the antiperistalsis, normally occurring in the ascending colon, is inhibited and is replaced by forward movements. The contents are thus hurried onwards towards the rectum. The entry of fæces into the rectum, particularly the lower part, excites the defæcation reflex. Unless voluntarily inhibited, a strong, massive contraction of the whole of the descending colon, pelvic colon, and rectum ensues, and their contents are expelled *per anum.* It is evident that under purgatives the contents of the descending colon will be more bulky than normal, since their hurried transit down the alimentary canal has not allowed of sufficient time for absorption of fluid, etc. The rectum will be distended unduly, and the stimulus exciting the defæcation reflex will be correspondingly great. Add to this the presence of a chemical irritant (the purgative) and it is easy to understand the irresistible call to stool that results. The question arises whether irritation in the upper part of the intestine can cause movements in the colon and rectum, or whether the reflex is purely local, except in the case of the defæcation reflex. It is well known that mental states affect the bowels; to most persons the ingestion of breakfast is a mild stimulus to defæcation. The extent of movement thus induced was shown by Hertz to be sufficient to move the contents of the transverse colon towards, or into, the descending colon. Wood found that section of the vagi prevented purgation, but his experiments are open to criticism. Hay showed that the hypodermic injection of salt solution might cause defæcation. These facts are difficult to explain unless a reflex mechanism be postulated. Radziejewski, by ligaturing the jejunum in dogs and administering purgatives above the point of obstruction, obtained evacuation of the bowels. Hess, on the other hand, by occluding the upper part of the small intestine in dogs with a rubber ball and introducing purgatives into the duodenum, never obtained purgation until some hours after the obstruction was removed. His protocols show, however, that most of his animals defæcated while the

obstruction still existed. It seems on the whole probable that distant reflexes assist defæcation, but that this effect is insignificant in comparison with the local response which occurs as the purgative passes along the bowel.

Some observers have thought that the purgatives also aid intestinal movements by acting directly on the muscle of the bowel after absorption. It is true that many members of the series act after subcutaneous injection, but it has also been shown that they are excreted into the bowel, and therefore have an opportunity of exerting their local irritant effect. Moreover, the purgatives as a class have no action on a length of intestine isolated from the body and suspended in an oxygenated Ringer's solution. Here there is every opportunity for a direct muscular effect to manifest itself, but practically none for demonstration of a local reflex caused by irritation of the mucous membrane, since the epithelium of the mucosa does not survive under these conditions.

Summing up, we may say that the rapid transit of intestinal contents observed under purgatives of this group is mainly due to frequent and powerful peristaltic movements, which are elicited through a local reflex by continuous irritation of the intestinal mucosa.

There has been much discussion concerning the origin of the water in the stool produced by purgation. Radziejewski, who showed that leucin, tyrosin and ferments were frequently present in such excreta, maintained that the hurried expulsion of the contents of the colon accounted for the presence of these abnormal constituents; as sufficient time for absorption of water, amino-acids, etc., was not allowed. Moreover, he did not find any increased secretion when purgatives were applied locally to the intestinal mucosa. Thiry and Brieger confirmed this point, but Lauder Brunton and others obtained different results, and concluded that these substances actively excite secretion.

These divergent results are partly a question of dosage. Large doses, as every one admits, cause a marked inflammatory exudation, and the line between this and secretion is not easy to define. Also the method of experiment is open to objection. The introduction of purgatives into washed-out loops of bowel does not imitate the true condition sufficiently closely; as will be seen later, the presence of bile may have a profound influence on the action of a purgative, and this probably affects the secretory action as well. Also, most of these experiments have been carried out on the small intestine, while it is the colon which is predominantly affected by purgatives. The amount of mucus which usually accompanies the stools after drastic purgatives, such as colocynth, is strong indication of a super-normal secretion.

In sifting the evidence it is as well to remember that the digestive secretions poured into the intestines amount to several litres per diem; so that a very slight hurrying of contents through the large bowel would account for the watery nature of the diarrhœic stool. Moreover, purgation in fasting animals is not attended with bulky fluid motions. Just as in the later stages of the effects of a large dose of a drastic purgative there is a great deal of tenesmus and straining, with very little result save the passage of mucus.

The balance of evidence indicates that the main bulk of the fluid is the result of incomplete absorption owing to the hurried expulsion of the contents of the colon, but that some increase of secretion of succus entericus, and of mucus from the large intestine, also occurs.

None of the purgatives are true cholagogues, but it has been shown by Stadelmann that bile is necessary for the action of a number; jalap resin, scammony resin, podophyllum and rhubarb, are without action in cases of complete biliary fistula. Bile probably acts as a solvent and brings the irritant into close contact with the mucous membrane.

Secondary Effects.—The irritation and increased muscular movements of the bowel cause a marked vaso-dilatation throughout the splanchnic area, and consequently a fall in general blood pressure. Associated with this there is usually some congestion of the pelvic viscera, which may increase the menstrual flow, and even cause abortion in pregnant women. The drastic purgatives remove a considerable amount of water from the body, and are occasionally used for that purpose.

The purgatives have very little action after absorption, though the anthracene group occasionally cause nephritic symptoms.

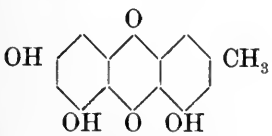
The rapid and frequent evacuation of the colon causes the expulsion of large numbers of bacteria; and in the treatment of intestinal disorders of bacterial origin better results are obtained with purgatives, particularly calomel or mercury, than with intestinal antiseptics alone.

There is no definite evidence of sensory nerve supply to the alimentary canal from the stomach to the last few inches of the rectum. Inflammation will, however, give rise to referred pain and tenderness over the abdomen, and colic is sometimes experienced under the action of a purgative. The mechanism of this pain sensation is not thoroughly understood, but it appears to be connected with excessive tension either in the intestine itself, the mesentery, or the peritoneum. Colic is due to strong local muscular contractions on intestinal contents, and the addition of hyoscyamus or atropine (see *Atropine*) to a purgative prescription diminishes this symptom to a great extent. Opium and morphia are occasionally employed,

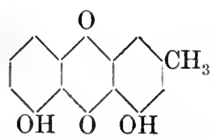
but they nearly always produce an after constipating effect.

1. **Substances acting on the Colon—sometimes called Anthracene Purgatives.**—Rhubarb, senna, aloes and cascara have been shown to contain various derivatives of anthraquinone. Their purgative properties are usually attributed to the presence of these principles. The chemical examination of these drugs is unfortunately very difficult, and the pure substances, when isolated, often do not represent the whole activity of the crude preparation. Aloin, for example, represents a fair proportion of the activity of aloes, but it appears to be less efficient than the original drug. Meyer showed that sodium carbonate and iron salts increased the purgative power of aloin. It is believed that aloin does not act *per se*, but that it undergoes some alteration (such as oxidation) in the intestine, which renders it purgative. Some change of this kind would account for the comparatively long time that aloes takes to produce its effect (twelve to twenty-four hours).

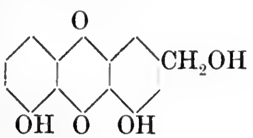
Emodin, chrysophanic acid, aloe-emodin, rhein, emodin-mono-methyl-ether, have been isolated from various members of this group. The relationship of some of these is seen in the following formulæ—



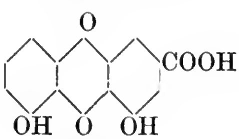
Emodin



Chrysophanic acid



Aloe-emodin



Rhein

Glucosides of the above are also known to exist and have been isolated in a pure state.

Tschirch believed these substances to be active, and supposed that the slow liberation of these and other oxyanthraquinones from glucosides in the intestine accounted for the activity of the various members of this group. This supposition can no longer be accepted, for Tutin and Clewer have shown, in the case of rhubarb, that all the glucosides, which they isolated in a pure state, were inactive, and that the only anthraquinone derivatives which were active, when purified, were aloe-emodin and chrysophanic acid. The most active constituent of rhubarb they found to be an intractable resin which was not glucosidic. This fact falls into line with Stadelmann's observation that the presence of bile is necessary for rhubarb to produce a purgative effect.

In cascara sagrada, although anthraquinone derivatives are known to be present, the pure active principle representing the activity has not yet been isolated.

From senna, an acidic glucoside, or mixture of glucosides, has been obtained—the so-called cathartinic acid. It is certainly an impure mixture.

It has been suggested that the low activity of the pure anthraquinones is due either to too rapid absorption, or insolubility in the absence of plant colloids and resins. Either of these is possible, but it is much more probable that in most cases the pure principle has not been isolated.

Senna and rhubarb impart a deep orange-yellow colour to the urine, and the addition of caustic alkali causes the development of a fine red colour. The chromagen of this reaction is acidic and ether-soluble; it is supposed to be some derivative of chrysophanic acid. Some members of this group, particularly aloes, cause acute nephritis in rabbits. In man the absorption is slight, and even if given hypodermically they are mostly excreted into the intestine, so that nephritic symptoms are rare. The possibility of nephritis should be borne in mind and their prolonged use discouraged. For occasional use they are, however, admirable purgatives; they are not irritant to the stomach, they are readily made palatable, and full doses are well borne. All members act principally on the large intestine. Senna was shown by Magnus, and later by Stierlin, to be very powerful in this respect; the entry of senna into the cæcum is followed, in a very short time, by strong intermittent contractions of the colon; aloes, on the other hand, produces a tonic contraction of the musculature, and hence the forward movement of contents is slower (Betz and Gebhardt). The tendency of aloes to cause colic and congestion of the intestinal vessels is thus explained. On account of this secondary vascular effect the use of aloes is contra-indicated in cases of hæmorrhoids and menorrhagia; on the other hand, such an effect may be valuable, as in amenorrhœa and allied conditions.

The association of purgative properties with the anthraquinone nucleus has led to the investigation of a number of synthetic substances of this nature. Vieth found that anthrapurpurine was the best of seven mild purgatives. The diacetyl derivative is known as "purgatin." "Exodin" is another synthetic derivative of anthraquinone which has been employed in therapeutics.

Phenolphthaleine is closely related to the anthraquinone series and has obtained a reputation as a laxative. It is perhaps the best of the synthetic purgatives of the kind. Some derivatives of phenolphthaleine also have purgative properties.

2. Substances acting on the Small and Large Intestine.—Castor oil consists for the most part of the glycerine ester of ricinoleic acid. The crude oil contains a little of the free acid and some other esters. Its purgative properties are due to the liberation of ricinoleic acid, an unsaturated fatty acid allied to oleic acid, in the intestine. Meyer showed that the free acid, its ethyl ester, or the free acid recovered from the amide, were all active. The saturated bromine compound, however, was not. Magnus showed that castor oil, when pure, in common with other neutral fats, lengthened the time during which food remained in the stomach. In the small intestine it greatly increases the rate of peristalsis. Apart from its nauseous flavour it is an excellent laxative, and large doses can be taken with impunity. Numerous devices are employed to render it more palatable, but none of them are entirely successful.

Croton oil is a complex mixture of fats. It contains a very powerful irritant and has been used as a vesicant or pustulant. It was believed at one time that its irritant and purgative properties were due to the presence of "crotonoleic acid" and its ester. Dunstan and Boole, however, by fractionating the so-called "crotonoleic acid," obtained a number of harmless fatty acids and an extremely powerful irritant resinous substance, which was not acidic or basic, and defied crystallisation.

Croton oil is not frequently employed in treatment, as for most purposes it is too powerful. The small dose ($\frac{1}{2}$–1 min.) makes it a convenient purgative for unconscious or imbecile subjects, and it is therefore occasionally employed in cerebral hæmorrhage, uræmia, eclampsia, and in the treatment of the insane.

From podophyllin a definite crystalline substance was isolated by Podwyssotzki, who named it podophyllotoxin. It is a powerful irritant, and given by the mouth or hypodermically causes purgation. Administered by the latter method it produces acute inflammation at the site of injection, and may even cause sloughing. The residual resin after separation of the podophyllotoxin is also active. A cholagogue effect has been attributed to podophyllotoxin, but its effects in this direction are meagre, and have been denied by some observers.

From *Ecballium Elaterium* a crystalline substance is fairly readily obtained—the elaterin of the 1898 pharmacopœia. It was, for some time, regarded as a single definite substance, but Power and Moore have recently shown that it is possible to separate two forms of elaterin from the crude product by fractional crystallisation. The two elaterins differ in optical properties, but have the same composition. A small quantity of dextrorotary elaterin (β-elaterin) was obtained, and this proved to be very much stronger than the original crude product. The pure lævorotatory body (α-elaterin) was almost devoid of activity. Unless special precautions are taken, the white clean-looking specimens of elaterin have poor purgative properties, and, apart from the specific optical rotation of a specimen of elaterin, there is no guide to its value as a purgative.

Colocynth was shown by Power and Rogerson to contain a small quantity of α-elaterin, and one or more water-soluble glucosides. The activity was found to be due to an amorphous alkaloid and a non-glucosidic resin. The statements of previous workers as to the presence of active glucosidic resins were not confirmed.

Jalap and *Scammony* yield resinous mixtures when suitably treated. These resins contain the whole activity of the crude drugs, but as they are complex mixtures they are unworthy of the special names which have been bestowed upon them.

The fact that the crystalline elaterin of the 1898 pharmacopœia, which is itself a highly active substance, owes its activity to the presence of a small quantity of β-elaterin, suggests that the resins, obtained from crude purgatives, owe their activity to the presence of small quantities of extremely powerful irritants. As this is possible, and even probable, deductions as to the nature of the active principle, drawn from the constitution of the decomposition products of the resins, are of minor interest to the pharmacologist.

Calomel is such an insoluble substance that it is surprising that it should have any action. It is, however, slowly absorbed in the body fluids, and may give rise to symptoms of mercurialism (see *Mercury*). It has been suggested that it unites with proteins of the tissues, forming a mercury albuminate, and in this way acts as an irritant to the intestinal mucosa. This supposition receives some support from the fact that diarrhœa is a prominent symptom in mercury poisoning. It is probable that the formation of a protein-mercury complex in the alimentary canal would be followed by local symptoms first. If, however, this complex cannot be excreted, absorption will take place and mercurialism result. And this is precisely what happens with calomel; if given in excessive doses, or if obstruction exist, symptoms of mercury poisoning develop. Were it not for this drawback it would be an ideal purgative; it is tasteless, does not cause irritation in the stomach, acts throughout large and small intestines, and is, in the great majority of cases, sufficiently powerful. In addition it exerts a mild antiseptic action, which is sometimes very desirable.

The purgatives of this group, with the exception of castor oil, may be termed drastic purgatives. They are, therefore, only used where severe purgation is desired, or where the con-

dition indicates that a milder remedy would be useless. In large doses they cause severe gastro-intestinal irritation, and may even produce acute hæmorrhagic inflammation of the intestine. It is desirable, in most cases, to follow the administration of one of these drastic purgatives with a saline draught some hours afterwards. Traces of the powerful irritant are thus washed out of the colon, and useless straining therefore obviated. If the saline be administered as soon as the first sensation of uneasiness is felt in the region of the descending colon, the whole evacuation occurs at one time, and is comparatively comfortable.

Group II.—Substances which induce Purgation by increasing the Water Content of the Alimentary Canal.

The members of this group are, for the most part, simple salts of organic and inorganic acids, and on this account are usually termed *Saline Purgatives*. Their characteristic action is the production of one or more profuse watery evacuations within two or three hours after oral administration.

There has been considerable discussion about the mode of action of this class of purgative and very divergent views have been held from time to time.

It is generally agreed that saline purgatives do not act in the same way as those previously described. It is true that concentrated solutions of the saline purgatives have irritant properties, and owing to this fact such solutions, or the salts themselves, when introduced into the stomach, cause uncomfortable sensations, nausea and even vomiting. But it has been shown by Otto and others that such solutions become diluted very quickly in the stomach, and that by the time the alimentary contents reach the jejunum they are nearly isotonic with the tissue fluids; and in approximately isotonic solution these substances have no irritant properties. Nevertheless the saline purgatives have been shown by several observers to increase the frequency and force of the peristalsis of the intestine. The diluted saline solution occupies a large volume and thus tends to distend the intestine. Distention of the intestine has been shown to be one means of exciting the peristaltic reflex, and the increased peristalsis can be accounted for in this manner. It has further been shown, by Cushny and Wallace and others, that the volume of intestinal contents reaching the colon is unusually large under this class of purgative; and, further, that the fluid which enters the large bowel contains a large proportion of the saline purgative. The bulky fluid contents of the large intestine excite muscular contractions as before, and, in due course, when the contents reach the pelvic colon and rectum, the defæcation reflex is elicited. The high proportion of a saline purgative which is excreted in the dejecta shows that these salts are absorbed with difficulty, and the facts outlined above indicate that the saline purgatives produce their effect by virtue of their power of attracting water. The mucous membrane of the intestine may be compared to a semi-permeable membrane in a simple osmosis experiment (see *Salt-Action*). A concentrated solution of a salt will be diluted, and a dilute solution will be concentrated, until the osmotic pressure of the solution balances the osmotic pressure of the tissues, plus the other forces which determine the absorption of water. If this point of view is correct, the potency of a saline purgative should depend on the difficulty with which it is absorbed from the alimentary canal; and this is, broadly speaking, found to be the case. The salts which are readily absorbed, as, for example, sodium chloride, do not cause purgation unless given in very large doses. Salts which are absorbed with difficulty, such as magnesium sulphate and sodium sulphate, cause purgation when given in comparatively small doses.

The factors which determine the absorption or non-absorption of salts are as yet imperfectly known. In solutions they are ionised, and the absorption of one ion may be more readily accomplished than another. In the case of magnesium sulphate, for example, the anion (SO_4 ion) is more readily absorbed than the kation. The anion is in large measure excreted by the kidney in union with another kation from the body; this naturally causes a diminution in the alkali content of the tissues. The kation is excreted in the fæces as carbonate or chloride. It is reasonable to suppose that the absorption of the various ions depends on the ease with which they can penetrate the cells of the mucous membrane. But why the cells of the intestinal mucosa should be permeable to some ions and impervious or relatively impervious to others in unknown.

Cushny and Wallace pointed out that in the case of the anions there was a parallelism between the insolubility of their calcium salts on the one hand and their purgative properties on the other. Attempts have also been made to connect the purgative properties of salts with their power of precipitating proteins. Again, the imbibition of water by colloids (such as gelatine and agar-agar) is profoundly influenced by the presence of salts; broadly speaking, those which are readily absorbed from the intestine increase the amount and rate of imbibition of water (Hofmeister, Pauly), and those which are absorbed with difficulty diminish it. But simple explanations along these lines all fail, because the saline purgatives are quite readily absorbed from other sites in the body, such as

the pleura, subcutaneous tissues, etc. Calcium, proteins and colloids are present in all cells, and if the absorption of these purgative salts were determined by one or more of these factors, then the rate and amount of absorption should be the same in the various sites of the body. As we have seen, this is not the case.

The theory outlined above is the one which is generally accepted, but other views have been held. Some observers believe that the saline purgatives act after absorption, and that the unabsorbed fraction of a given dose is without action. Experiments are recorded where the application of saline solutions to the intestines, or their hypodermic or intravenous administration, has been followed by increased peristalsis and purgation (MacCallum). Frankl and Auer failed to confirm this; indeed, they frequently noticed constipation after intravenous administration of salines to animals. Hay showed that the hypodermic administration of saline purgatives only caused purgation if the injection were made over the abdomen. Hertz, Cook and Schlesinger, working on man, as a result of X-ray examinations and analyses of fæces, concluded that the absorbed salt was the active fraction. They found that purgation occurred before the bismuth travelled through the alimentary canal, and that the purgative diarrhœic stool contained less sulphate than the following normal motion.

Padtberg, working on cats, failed to confirm these X-ray results, and came to exactly the opposite conclusion. Ury, who recently carried out elaborate analyses of fæces, failed to confirm the analytical results. He found that 50–70 per cent. of the administered sulphate was excreted in the first diarrhœic stool, and that carmine particles, given with the saline draught, could be detected in the first motion.

On the isolated intestinal muscle these salts are without action in isotonic solution, and are depressant in hypertonic solution.

Some of these observations are very difficult to reconcile with one another. The discrepancies are no doubt in part due to differences in dosage. Hertz and his co-workers used doses of 4–5 gm. Ury, Padtberg and others 20–30 gm. It is possible that small doses can cause defæcation, either reflexly, or during excretion of part of the absorbed salt into the rectum; but there can be no doubt that the massive dose acts by flushing the alimentary canal in the manner first described.

The origin of the fluid which is turned out into the alimentary canal on administration of a concentrated solution of a saline purgative has been variously regarded as a secretion, as a transudate, or an exudate. Its chemical composition shows that it is very similar to succus entericus, but is poorer in ferments (Hay, Ury).

The passage of water into the alimentary canal was shown by Hay to be accompanied by a temporary rise in the concentration of the blood. Thus a 20 per cent. solution of sulphates might temporarily raise the number of red corpuscles from 5–6½ millions. A 3–5 per cent. solution, on the other hand, was without effect in this direction. These facts show that the saline purgatives are of service in depleting the body of water. The rapid transit of food material along the alimentary canal diminishes the absorption of food material, and, in the case of magnesium salts, a certain proportion of insoluble magnesium soaps are formed, and thus the absorption of fats is diminished.

The flushing of the alimentary tract washes out large numbers of bacteria and thus causes a partial disinfection of the same. In addition the bacteria may reduce some of the sulphate to sulphide, which, on the one hand, excites peristalsis, and, on the other, acts as an antiseptic. Powdered sulphur produces its effect in the same way, namely through the formation of sulphuretted hydrogen by bacterial action in the intestine.

Group III.—Substances which stimulate the Neuromuscular Mechanism of the Alimentary Canal

This group comprises a very large number of substances, but very few of them are used in therapeutics for their purgative action.

Pilocarpine and physostigmine cause purgation by stimulating the peripheral motor apparatus of the intestines; they thus evoke powerful peristaltic contractions throughout the alimentary canal. Their effect on the heart, salivary secretion, etc., almost debars their use in medicine for this purpose. They are occasionally employed when other remedies fail and are frequently employed in veterinary practice (see *Pilocarpine* and *Physostigmine*).

Pituitary extract has been found to be of great value in cases of intestinal atony, and it certainly has an effect on the muscle of the alimentary canal of man in such conditions.

This action on the intestinal musculature varies considerably in different animals. In the dog and cat the effect is very small, but in the rabbit a well-marked stimulating effect can readily be demonstrated. In man the beneficial results which have been observed clinically may in part be due to the improvement in the general condition (see *Pituitary Extract*).

Numerous other substances, such as the digitalis series of drugs and some heavy metals, may cause diarrhœa; as, however, they are not employed in therapeutics as purgatives, the reader is referred to the other sections of this volume.

Mechanical Methods of inducing Purgation.—A brief consideration of the mechanism of defæcation and what has been said regarding

the action of purgatives would lead one to expect that the introduction of fluids and irritants into the large intestine *per anum* should cause evacuation of the bowel. This simple method of inducing defæcation is frequently employed. Suppositories and enemata act on these lines; the more powerful the irritant and the more bulky the enema the greater the stimulus to defæcation. Enemata are usually composed of water, soap, glycerin or other mild irritant, and by their use the lower part of the colon and rectum are readily emptied. But they have only a limited application, because they usually do not affect the ascending and transverse colons. An enema of sufficient volume to induce evacuation of the whole colon and rectum produces considerable discomfort; and in most cases has no superiority over a purgative. In cases where there are masses of hard fæces an enema may render them softer and more easily expelled: for this purpose olive oil is occasionally employed.

To mechanical methods of promoting regular defæcation belong also those procedures which aim at increasing the bulk and softening the consistency of the fæces by administering by the mouth substances which are soft, bulky and unaffected by the digestive ferments. Agar-agar, a gelatinous carbohydrate from seaweeds, has been used with success for this purpose, and purified liquid paraffin has recently received wide recommendation for similar use. Fruits and vegetables with a high proportion of cellulose are for similar reasons of great importance in the dietetic treatment of constipation.

Cholagogues.—A cholagogue is a substance which increases the secretion of bile. Purgatives were formerly believed to be cholagogues because the diarrhœic stool which they produced was shown to contain more bile constituents than normal. Direct experiment on men and dogs, with complete biliary fistulæ, have since shown that purgatives do not increase the secretion of bile, and may in fact have the opposite effect. The rapid evacuation of the contents of the intestines certainly increases the amount of bile eliminated from the body, as sufficient time is not allowed for the absorption of bile salts, which normally occurs. If excess of bile salts is considered harmful a purgative will aid in their excretion, but if a deficiency in biliary secretion exists the only certain remedy at our disposal is bile salts. All observers are agreed that they greatly increase the amount of bile. This is brought about by absorption of the bile salts in the intestine and their secretion into the biliary ducts by the liver. In addition to this, some of the most important constituents of bile are supplied directly, for although the bile salts of various species of animals differ somewhat in character and composition they are still able to take the place of the salts normally secreted in man.

In addition to their cholagogue action, bile salts produce a mild laxative effect when given by mouth. Their importance to the animal economy lies in the fact that the absorption of fats is greatly improved by their presence. Injected hypodermically or intravenously they have a depressant action on the central nervous system and render the heart-beat slow and feeble.

Turpentine, olive oil, salicylates, benzoates, podophylloresin and natural waters have been found to have slight cholagogue actions by some observers. The effects they produce are so small that they are of doubtful therapeutic importance in this connection; indeed, other observers have failed to demonstrate any increase in the amount of bile as a result of their administration.

Preparations

Note.—Preparations marked † are those more frequently employed.

Senna.

Sennæ Folia (B.P., U.S.P.); the dried leaflets of *Cassia acutifolia*, or *Cassia angustifolia*.

Syrupus Sennæ (B.P., U.S.P.). ½–2 fl. dr. (2–8 ml.).

†Infusum Sennæ (B.P.). ½–2 fl. oz. (15–60 ml.).

†Confectio Sennæ (B.P., U.S.P.). 60–120 gr. (4–8 g.). (Senna, figs, prunes, liquorice, tamarinds, coriander and sugar.)

†Mistura Sennæ Composita (B.P.). 1–2 fl. oz. (30–60 ml.). (Senna, magnesium sulphate, liquorice, cardamoms, aromatic spirit of ammonia.)

Infusum Senna Compositum (U.S.P.). 2–4 fl. oz. (60–120 ml.). Similar to above.

Tinctura Sennæ Composita (B.P.). ½–4 fl. dr. (2–16 ml.).

Sennæ Fructus (B.P.).

Aloes.

Aloe (B.P., U.S.P.). Curaçao, Socotrine, or Zanzibar Aloes. 2–5 gr. (12–30 cg.).

Aloinum (B.P., U.S.P.). ½–2 gr. (3–12 cg.).

†Extractum Aloes (B.P., U.S.P.). 1–4 gr. (6–25 cg.).

Decoctum Aloes Compositum (B.P.). ½–2 fl. oz. (15–60 ml.).

Pilula Aloes (B.P., U.S.P.). 4–8 gr. (25–50 cg.).

†Pilula Aloes et Ferri (B.P., U.S.P.). 4–8 gr. (25–50 cg.).

Pilula Aloes et Asafetidæ (B.P.). 4–8 gr. (25–50 cg.).

Pilula Aloes et Myrrhæ (B.P., U.S.P.). 4–8 gr. (25–50 cg.).

Tinctura Aloes (U.S.P.). 30 min. (2 ml.).

Aloes is also combined with other purgatives, Pilula Colocynthidis et Hyoscyami, Pilula Colocynthidis Composita, etc.

Cascara.

Cascara Sagrada (B.P.), Rhamnus Purshiana (U.S.P.); dried bark of *Rhamnus Purshianus*.

†Extractum Cascaræ Sagradæ Liquidum (B.P.). ½–1 fl. dr. (2–4 ml.).

†Fluidextractum Rhamni Purshianæ (U.S.P.). 15 min. (1 ml.).

Extractum Cascaræ Sagradæ Siccum (B.P.). 2–8 gr. (12–50 cg.).

Syrupus Cascaræ Aromaticus (B.P.). ½–2 fl. dr. (2–8 ml.).

Rhubarb.

Rhei Rhizoma (B.P.), Rheum (U.S.P.), the root of *Rheum officinale*. 3–30 gr. (2–20 dg.).

Extractum Rhei (B.P., U.S.P.). 2–8 gr. (12–50 cg.).

†Pilula Rhei Composita (B.P., U.S.P.). 4–8 gr. (25–50 cg.). (Rhubarb, aloes, myrrh, peppermint oil.)

†Pulvis Rhei Compositus (B.P., U.S.P.). Gregory's Powder. 10–60 gr. (6–40 dg.). (Rhubarb, magnesia and ginger.)

†Tinctura Rhei Composita (B.P.). ½–4 fl. dr. (2–16 ml.).

Syrupus Rhei (B.P., U.S.P.). ½–2 fl. dr. (2–8 ml.).

Infusum Rhei (B.P.). ½–1 fl. oz. (15–30 ml.).

Mistura Rhei et Sodæ (U.S.P.). 1 fl. dr. (4 ml.). (Bicarbonate of soda, ipecacuanha, peppermint, glycerin and rhubarb.)

Colocynth.

Colocynthidis Pulpa (B.P.), Colocynthis (U.S.P.); dried pulp of *Citrullus Colocynthis*.

Extractum Colocynthidis Compositum (B.P., U.S.P.). 2–8 gr. (12–50 cg.). (Colocynth, aloes, scammony and cardamoms.)

†Pilula Colocynthidis Composita (B.P.). 4–8 gr. (25–50 cg.). (Colocynth, aloes, scammony, potassium sulphate and clove oil.)

†Pilula Colocynthidis et Hyoscyami (B.P.). 4–8 gr. (25–50 cg.).

Extractum Colocynthidis (U.S.P.). ½ gr. (3 cg.).

Pilulæ Catharticæ Compositæ (U.S.P.). (Colocynth, jalap, gamboge, calomel.)

Pilulæ Catharticæ Vegetabiles (U.S.P.). (Colocynth, jalap, leptandra, podophyllum, hyoscyamus and peppermint oil.)

Podophyllum.

Podophylli Rhizoma (B.P., U.S.P.); the rhizome and roots of *Podophyllum peltatum*.

Fluidextractum Podophylli (U.S.P.). 8 min. (5 dl.).

†Podophylli Resina (B.P., U.S.P.). ¼–1 gr. (16–60 mg.).

Tinctura Podophylli (B.P.). 5–15 min. (3–10 dl.).

Podophylli Indici Rhizoma (B.P.).

Podophylli Indici Resina (B.P.). ¼–1 gr. (16–60 mg.).

Tinctura Podophylli Indici (B.P.). 5–15 min. (3–10 dl.).

Jalap.

Jalapa (B.P., U.S.P.); tubercules of *Ipomœa Purga*.

Jalapæ Resina (B.P., U.S.P.). 2–5 gr. (12–30 cg.).

†Pulvis Jalapæ Compositus (B.P., U.S.P.). 10–60 gr. (6–40 dg.). (Jalap and bitartrate of potash.)

Tinctura Jalapæ (B.P.). ½–1 fl. dr. (2–4ml.).

Tinctura Jalapæ Composita (B.P.). ½–1 fl. dr. (2–4 ml.).

Kaladana (B.P.). 30–45 gr. (2–3 g.).

Pulvis Kaladanæ Compositus (B.P.). 10–60 gr. (6–40 dg.).

Tinctura Kaladanæ (B.P.). ½–1 fl. dr. (2–4 ml.).

Kaladanæ Resina (B.P.). 2–8 gr. (12–50 cg.).

Turpethum (B.P.). 5–20 gr. (3–12 dg.).

Tinctura Jalapæ Composita (B.P.). ½–1 fl. dr. (2–4 ml.).

Scammony.

Scammoniæ Radix (B.P.). Dried root of *Convolvulus Scammonia*.

Pulvis Scammoniæ Compositus (B.P.). 10–20 gr. (6–12 dg.). (Scammony, jalap and ginger.)

Scammoniæ Resina (B.P.). 4–8 gr. (25–50 cg.).

Ipomœæ Radix (B.P.); a source of Scammoniæ Resina.

Elaterin.

Elaterinum (U.S.P.). $\frac{1}{40}$–$\frac{1}{10}$ gr. (1·5–6 mg.).

Trituratio Elaterini (U.S.P.). ½ gr. (30 mg.).

Gamboge.

Cambogia (U.S.P.). Gum resin of *Garcinia Hanburyi*. ½–2 gr. (3–12 cg.).

Euonymus.

Euonymi Cortex (B.P., U.S.P.). Dried root bark of *Euonymus atropurpureus*.

Extractum Euonymi (B.P., U.S.P.). 1–2 gr. (6–12 cg.).

Fluidextractum Euonymi (U.S.P.). 8 min. (5 dl.).

Castor Oil.

Oleum Ricini (B.P., U.S.P.). A fixed oil expressed from seeds of *Ricinus communis* 1–8 fl. dr. (4–30 ml.).

Mistura Oleui Ricini (B.P.). 1–2 fl. oz. (30–60 ml.). Emulsion of castor oil, flavoured.

Croton Oil.

Oleum Crotonis (B.P.); Oleum Tiglii (U.S.P.). A fixed oil expressed from seeds of *Croton Tiglium.* ½–1 min. (3–6 cl.).

Linimentum Crotonis (B.P.).

Phenolphthaleinum (B.P.). "Purgen." 2–5 gr. (12–30 cg.).

Saline Preparations.

†Sodii Sulphas (B.P., U.S.P.). (Glauber's salt). $Na_2SO_4 10H_2O$. 30–240 gr. (2–16 g.).

Sodii Sulphas Effervescens (B.P.). 60–240 gr. (4–16 g.). (Sodium sulphate, sodium bicarbonate, citric and tartaric acids.)

Sodii Phosphas (B.P., U.S.P.). Na_2HPO_4-$12H_2O$. 30–240 gr. (2–16 g.).

Sodii Phosphas Effervescens (B.P., U.S.P.). 60–240 gr. (4–16 g.).

Liquor Sodii Phosphatis Compositus (U.S.P.). 2 fl. dr. (8 ml.).

Sodii et Potassii Tartras (B.P., U.S.P.). Soda Tartarata. Rochelle Salt, $NaKC_4H_4O_6$-$4H_2O$. 120–240 gr. (8–16 g.).

†Pulvis Sodæ Tartaratæ Effervescens (B.P.). Pulvis Effervescens Compositus (U.S.P.). Two powders: Blue—Rochelle salt 7·5 g., sodium bicarbonate 2·5 g. White—Tartaric acid 2·5 g.

†Magnesii Sulphas (B.P., U.S.P.). Epsom salts. $MgSO_4 7H_2O$. 30–240 gr. (2–16 g).

Magnesii Sulphas Effervescens (B.P., U.S.P.). 60–480 gr. (4–32 g.).

Magnesia Levis (B.P., U.S.P.). MgO.

Magnesia Ponderosa (B.P., U.S.P.). MgO.

Magnesii Carbonas (U.S.P.). $(MgCO_3)_4.Mg(OH)_2 5H_2O$.

Magnesii Carbonas Levis. Magnesii Carbonas Ponderosa (B.P.). $(MgCO_3)_3Mg(OH)_2 4H_2O$.

The last five are insoluble powders.

Dose: 5–60 gr. (3–40 dg.).

Liquor Magnesii Bicarbonatis (B.P.). 1–2 fl. oz. (30–60 ml.).

Liquor Magnesii Citratis (U.S.P., B.P.C.). 5–10 fl. oz. (100–300 ml.).

Lithii Citras Effervescens (B.P., U.S.P.). 60–120 gr. (4–8 g.). Lithium citrate, sodium bicarbonate, tartaric acid, citric acid.

Numerous unofficial preparations of salines are also frequently employed. They are for most purposes best administered in dilute form. Many natural waters such as Carlsbad, Hunyadi-Janos, etc., contain various salts (sulphates, etc.) which produce laxative effects.

Cholagogue *Fel Bovinum Purificatum* (B.P., U.S.P.). (Purified Ox Bile) 5–15 gr. (3–10 dg).

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P. P. L.

SIMPLE BITTERS

The **simple bitters** form an ill-defined group whose members have little resemblance except that they contain substances having a bitter taste and no other very pronounced physiological activity. As a class, the alkaloids are possessed of an intensely bitter taste, and preparations of quinine and nux vomica are sometimes employed in small doses as bitters, but in general they are not included in this group owing to their possessing marked specific activities in therapeutic doses. Certain alkaloids, *e.g.* berberine, have no special physiological properties except in very large doses, and in consequence preparations containing them are often used simply as bitters. The majority of the bitters consist of glucosides, weak acids and neutral principles such as quassin and columbin.

The bitters are used in medicine in order to improve appetite. In this respect they are undoubtedly of great value, although their mode of action is not definitely settled.

Numerous researches have been carried out from time to time in order to determine their physiological activity, but there is much contradiction in the literature of the subject. When given by the mouth bitters increase the flow of saliva and inhibit that of gastric juice for a time, but later the flow is increased. Such an action is of value in chronic gastritis, but in hyperchlorhydria tends to produce an aggravation of the symptoms. In vitro the influence on the digestive enzymes is commonly inhibitory, probably the result of the tannin which most preparations contain. In animals there is some evidence that the movements of the stomach and intestine are increased, and there may be increased flow of intestinal juices under the influence of large doses.

The unsatisfactory state of our knowledge of

the subject is probably due to the lack of a sufficient number of observations on man. Pawlow and his school showed clearly how important is the psychical factor in causing secretion in the stomach. Thus in dogs in whom an œsophageal fistula had been made so that none of the food swallowed was able to enter the stomach, there was an active secretion of gastric juice when appetising food was swallowed, and even when the animal's appetite was stimulated by the sight and smell of food. In such animals, the previous administration of bitters enhances the effect of this sham feeding, and since none of the drug could have reached the stomach it follows that the effect is the result of a psychic stimulus. In man, also, it is probable that the psychic element is the cause of the improvement; the chief common attribute possessed by the various members of this group is the bitter taste. The patient feels his appetite stimulated and takes his meal with added interest and relish and thus starts the chain of reflex processes which has as its beginning an efficient secretion of gastric juice. The first products of digestion cause the production of gastric secretin, which chemically stimulates the cardiac and fundus glands to secrete further quantities of juice; and the acid so poured out, when it reaches the duodenum, calls forth the production of secretin and thus ensures an adequate flow of pancreatic and intestinal juices. In animals excessive doses of some bitters have given rise to toxic symptoms, such as are seldom observed in man. Quassin is said to cause dryness and burning in the throat; berberine causes abdominal pain and purging when administered by the mouth, paralysis of the hind limbs and failure of the respiratory centre when injected intravenously.

Preparations

Gentianæ Radix (B.P.), Gentian (U.S.P.), the dried rhizome of *Gentiana lutea*, contains three bitter principles and a small quantity of tannin.

Extractum Gentianæ (B.P., U.S.P.).
Dose: 2–8 gr. (12–50 cg.). The extract is used as a pill excipient.

Fluidextractum Gentianæ (U.S.P.).
Dose: 15 min. (1 ml.).

Infusum Gentianæ Compositum (B.P.).
Dose: ½–1 fl. oz. (15–30 ml.). Contains also bitter orange and lemon. It is the most widely used preparation.

Infusum Gentianæ Compositum Concentratum. (B.P.C.).
Dose: ½–1 fl. dr. (2–4 ml.). When diluted with seven parts of distilled water yields a product closely resembling the compound infusion.

Mistura Gentianæ Acida (B.P.C.).
Dose: ½–1 fl. oz. (15–30 ml.). Contains about 2 parts per 100 of diluted nitro-hydrochloric acid.

Mistura Gentianæ et Sodæ (B.P.C.).
Dose: ½–1 fl. oz. (15–30 ml.). Contains 3 per cent. of sodium bicarbonate.

Tinctura Gentianæ (B.P.C.).
Dose: ½–1 fl. dr. (2–4 ml.).

Tinctura Gentianæ Composita (B.P., U.S.P.).
Dose: ½–1 fl. dr. (2–4 ml.).

Quassiæ Lignum (B.P., U.S.P.). The wood of *Picræna excelsa*, a Jamaica tree. The wood contains several bitter principles; its preparations are free from tannin, so may be prescribed with iron.

Extractum Quassiæ (U.S.P.).
Dose: 1–3 gr. (6–20 cg.).

Fluidextractum Quassiæ (U.S.P.).
Dose: 5–30 min. (3–18 dl.).

Infusum Quassiæ (B.P.). Made with cold water.
Dose: ½–1 fl. oz. (15–30 ml.).

Infusum Quassiæ Concentratum (B.P.C.).
Dose: ½–1 fl. dr. (2–4 ml.). Yields on dilution a product closely simulating the infusion, but containing about 2–5 per cent. alcohol.

Tinctura Quassiæ (B.P., U.S.P.).
Dose: ½–1 fl. dr. (2–4 ml.). In the United States the tincture is prepared approximately twice as strong and the average dose is 30 min. (2 ml.).

Calumbæ Radix (B.P., U.S.P.). The dried root of *Jateorhiza Columba*. Contains a bitter principle, columbin, the alkaloid berberine and a moderate amount of starch, but no tannin.

Fluidextractum Calumbæ (U.S.P.).
Dose: 15–30 min. (1–2 ml.).

Infusum Calumbæ (B.P.). Made with cold water.
Dose: ½–1 fl. oz. (15–30 ml.).

Infusum Calumbæ Concentratum (B.P.C.).
Dose: ½–1 fl. dr. (2–4 ml.). Is a more satisfactory preparation than the above.

Tinctura Calumbæ (B.P., U.S.P.).
Dose: ½–1 fl. dr. (2–4 ml.).

Chirata (B.P., U.S.P.). The dried plant, *Swertia Chirata*, contains ophelic acid and a glucoside chiratin. Its preparations are free from tannin.
Dose: 5–30 gr. (½–2 g.).

Fluidextractum Chiratæ (U.S.P.).
Dose: 5–15 min. (3–10 dl.).

Infusum Chiratæ (B.P.).
Dose: ½–1 fl. oz. (15–30 ml.).

Infusum Chiratæ Concentratum (B.P.C.).
Dose: ½–1 fl. dr. (2–4 ml.).

Tinctura Chiratæ (B.P.).
Dose : ½–1 fl. dr. (2–4 ml.).

Taraxaci Radix (B.P., U.S.P.), the root of the common dandelion. It is used both fresh and dried, as a bitter and mild laxative.

Elixir Taraxaci Compositum (B.P.C.).
Dose : ½–2 fl. dr. (2–8 ml.). Contains orange, cinnamon and other carminatives.

Extractum Taraxaci (B.P., U.S.P.).
Dose : 5–15 gr. (3–10 dg.).

Fluidextractum Taraxaci (U.S.P.).
Dose : 1–3 fl. dr. (4–12 ml.).

Mistura Taraxaci Acida (B.P.C.).
Dose : ½–1 fl. oz. (15–30 ml.). Contains infusion of calumba.

Succus Taraxaci (B.P.). Prepared by adding alcohol to the fresh juice.
Dose : 1–2 fl. dr. (4–8 ml.).

Berberis (B.P., U.S.P.), the dried stem or rhizome of various species of Berberis. Contains berberine, tannin and other substances.

Fluidextractum Berberidis (U.S.P.).
Dose : 30 min. (2 ml.).

Tinctura Berberidis (B.P.).
Dose : ½–1 fl. dr. (2–4 ml.).

Pareira (U.S.P.). Contains an alkaloid buxine.

Fluidextractum Pareiræ (U.S.P.).
Dose : 30 min. (2 ml.).

Serpentariæ Rhizoma (B.P., U.S.P.). The rhizome of *Aristolochia Serpentaria* or *reticulata*. Contains a bitter principle, volatile oil and tannin.

Infusum Serpentariæ Concentratum (B.P.C.).
Dose : ½–1 fl. dr. (2–4 ml.).

Tinctura Serpentariæ (B.P.).
Dose : ½–1 fl. dr. (2–4 ml.).

Cascarilla (B.P.). Dried bark of *Croton Eluteria*.
Infusum Cascarillæ (B.P.). ½–1 fl. oz. (15–30 ml.).
Infusum Cascarillæ Concentratum (B.P.C.). ½–1 fl. dr. (2–4 ml.).
Mistura Cascarillæ Composita (B.P.C.). ½–1 fl. oz. (15–30 ml.).
Tinctura Cascarillæ (B.P.). ½–1 fl. dr. (2–4 ml.).
Aurantii Cortex Siccatus (B.P., U.S.P.). Orange Peel.
Fluidextractum Aurantii Amara (U.S.P.). 15 min. (1 ml.).
Infusum Aurantii (B.P.). ½–1 fl. oz. (15–30 ml.).
Infusum Aurantii Compositum (B.P.). ½–1 fl. oz. (15–30 ml.).
Tinctura Aurantii Amara (U.S.P.). 1 fl. dr. (4 ml.).
Aurantii Cortex Recens (B.P.).
Syrupus Aromaticus (B.P.). ½–1 fl. dr. (2–4 ml.).
Syrupus Aurantii (B.P.). ½–1 fl. dr. (2–4 ml.).
Tinctura Aurantii (B.P.). ½–1 fl. dr. (2–4 ml.).
Vinum Aurantii (B.P.).
Aqua Aurantii Floris (B.P.).
Syrupus Aurantii Floris (B.P.). ½–1 fl. dr. (2–4 ml.).
Aurantii Cortex Indicus (B.P.). Indian Orange Peel.
Limonis Cortex (B.P., U.S.P.). Lemon Peel.
Syrupus Limonis (B.P.). ½–1 fl. dr. (2–4 ml.).
Tinctura Limonis (B.P., U.S.P.). ½–1 fl. dr. (2–4 ml.).

The chief use of the bitters is to stimulate appetite and digestion; this they do reflexly from their stimulation of the nerves of taste. They are of greatest value to convalescents and to patients suffering from chronic gastritis in whom there is deficient secretion of hydrochloric acid. In that form of dyspepsia associated with excessive secretion of acid (hyperchlorhydria) they tend to aggravate the symptoms. If, as appears to be the case, the sole action of bitters is through the nerves of taste, the administration of the solid extracts of gentian and quassia in the form of pills is unlikely to produce any effect. Gentian, calumba, quassia and chirata are the bitters most commonly prescribed, and of these gentian is by far the most important. Preparations of calumba, quassia and chirata contain little or no tannin and consequently are compatible with iron preparations. The tincture and infusion are the preparations most commonly employed.

Infusion of quassia is widely used as an enema in the treatment of threadworms in children. When prescribed for this purpose care should be taken that it is prepared fresh and not by dilution of the concentrated infusion. The latter contain a considerable proportion of alcohol (20 per cent.), and sufficient may be absorbed from the rectum to give rise to serious symptoms of poisoning. P. H.

CHARCOAL

Charcoal as used in pharmacy and medicine is derived from two sources, animal and vegetable. The animal variety is most commonly prepared by heating bones with the admission of but limited quantities of air; the resulting product consists chiefly of mineral substances such as calcium phosphate and contains about 10 per cent. of carbon with a small quantity of nitrogen in an unknown but very stable combination. On boiling with hydrochloric acid the greater part of the mineral matter is dissolved out and the resulting product is known as "purified animal charcoal." For special purposes charcoal prepared from blood is preferred owing to its greater power of decolorising solutions. Vegetable charcoal is prepared by heating wood, usually willow or poplar, either in retorts or by burning it in

stacks covered with sods and earth so as greatly to limit the admission of air. If desired the mineral matter may be removed by treatment with hydrochloric acid.

Charcoal possesses many curious properties, many of which are referable to the finely divided state in which it exists. Thus it rapidly removes colouring matter and some alkaloids from solution. Wood charcoal is of less value for decolorisation than the animal variety. It also has the property of condensing gases on its surface, though it appears to lose it when wet. The condensed gas can then be given up in an active form capable of destroying many unstable organic substances. In virtue of these properties charcoal, especially animal charcoal, is used as an antidote to many alkaloids and poisonous fungi, and also is of great value as a deodorant.

Charcoal is used in therapeutics externally and internally. Externally as a dressing to foul ulcerating surfaces it is very efficacious in rendering them sweet and clean; internally it is used chiefly in the treatment of various forms of dyspepsia, especially where flatulence and eructation are prominent symptoms. It is quite possible that its action may be largely mechanical in forming a protective coating to the mucous membrane of the stomach, though the improvement which frequently follows its administration is such as to incline one to the view that the chemical action of the occluded oxygen is an important factor.

Carbo Ligni (B.P., U.S.P.) is usually administered in cachets or lozenges and is a constituent of certain proprietary biscuits. A single large dose is commonly administered in order to indicate by the blackening of the fæces the rate at which foodstuffs are passing through the gut.

Dose: 60–120 gr. (4–8 g.). P. H.

SAPONINS

Source and Distribution.—The saponins form a sub-division of the bodies known as glucosides and may be rightly grouped under the name sapo-glucosides (Moore). The sapo-glucosides are widely distributed in the vegetable kingdom; they have been recognised in more than seventy families of mono- and dicotyledonous plants and ferns distributed all over the earth, and may occur in almost any part of the plant, *e.g.* in the root of Senega, Saponaria, Chamælirium; in the tuberous root of the Cyclamen; in the bark of Quillaia and Guaiacum; in the fruit of Sapindus; in the seed of Æsculus, Thea, Entada, Agrostemma; in the stalk of Dulcamara; in the leaf of Guaiacum. It seems probable that they are formed in the leaves and stored up in other organs. They may be present in quite large quantities, Laves (2) found 13 per cent. in the horse-chestnut. Though they have several properties in common, the sapo-glucosides from various plants are not necessarily identical, and indeed the same plant may contain more than one saponin.

Nomenclature.—With reference to the nomenclature of these bodies there appears to have been some misunderstanding as to the use of the terms saponin and sapotoxin. As all saponins are more or less toxic the retention of the name sapotoxin as indicating a group to be distinguished from saponins seems superfluous, if however, it should appear convenient to have such a means of differentiating, it would be best to follow Kobert (3) and when more than one saponin is present in a plant, to call the more toxic a sapotoxin prefixing the source, so quillaia-sapotoxin would indicate the more poisonous of the two sapo-glucosides present in quillaia.

Preparation.—Schrader's method, so-called (see Kobert (3) *l. c.* p. 146). The dried and coarsely powdered leaves or other parts of the plant are thoroughly exhausted with boiling 90 per cent. alcohol, the alcoholic extracts united, evaporated, dissolved again with the aid of heat in 90 per cent. alcohol and filtered hot; on cooling some saponin falls out, and the precipitation can be completed by adding excess of ether (Gehlen (4)); the precipitate is then well washed with ether. The saponin thus obtained is more or less coloured and impure. As most of the saponins are readily soluble in water the alcohol-ether precipitate may be extracted with water and the undissolved impurities filtered off. There are, however, a few saponins which are insoluble in water but soluble in cold strong alcohol (Flückiger (5)).

Kobert's (6, p. 7) lead method may be used to effect a further purification and separation. The watery decoction or alcoholic extract is neutralised and precipitated with neutral lead acetate, which throws down any acid saponins that may be present, the filtrate is then treated with basic lead acetate with which the neutral saponins fall out. The lead compound is decomposed with H_2S and the mixture, after the addition of alcohol, filtered. The precipitate thus obtained is thoroughly extracted with boiling alcohol and the alcohol extract precipitated with ether. By this means Kobert (6, p. 7) was able to demonstrate the existence of acid and neutral saponins. Barium method: precipitation of concentrated aqueous solutions of saponins with solution of barium hydrate. Unfortunately the activity of the saponins is materially affected by this process (Kobert (6, p. 6)). It appears that the fatty acid group, whose presence in the saponin molecule is necessary for the activity of the saponin, is removed by the barium.

Magnesium method (Greene (7)): the concentrated watery decoction is treated with magnesium hydroxide, the mixture evaporated to dryness and the dry remainder powdered and extracted with hot alcohol.

Ammonium sulphate method (Kobert (6, p. 21)): the filtered and concentrated decoction is treated with saturated solution of ammonium sulphate. The amount of salt solution necessary varies with different saponins, the acid saponins are especially easily precipitated, the neutral ones with more difficulty or even not at all.

Shaking out methods with ether, chloroform, benzol or petrol ether are not available, but according to Brunner (8) phenol may be used in this way.

Physical Properties.—The saponins have for the most part only been obtained in amorphous form, but arhyræscin, cainca-saponin, digitonin, dioscin, parillin, sapolin and sarsasaponin form crystals.

The watery solutions of saponins all froth readily, hence decoctions of plants, or parts of plants, containing saponins have been used for washing from time immemorial (the name quillaia means the washing wood) and are still so used in certain industries. They have the advantage over soap that they do not affect even the most sensitive colours nor harm the most delicate wool or silk fabrics. The frothing or lather is quite evident even in very dilute solutions, 1 in 10,000 and more, and saponins have been added to lemonade and other effervescing drinks in order to give them a more permanent froth.

All soluble saponins reduce the surface tension of fluids to which they are added, and hence may, under certain conditions, favour absorption.

In consequence of the presence of sugar in their molecule the saponins are all active to light and may turn the polarised ray either to the right or left.

The saponins do not dialyse with any readiness and are not usually absorbed in any important quantity from the intestinal canal, with the exception of the saponin from Agrostemma which appears to be rather readily taken up.

If precipitated they are apt to carry down any colouring matter which may be present, and some of them at any rate have the remarkable property of attracting and holding colouring matters, so that if a solution of saponin is placed in a dialysing thimble and immersed in a solution of methylene blue after some hours the external solution will have lost almost all colour and that within the thimble will be deep blue (Kobert (6, p. 36)). The saponins readily form emulsions and have great powers of holding insoluble bodies, very finely divided, in suspension, and they are often used for these reasons in the arts and in medicine. It is said that in making an infusion of digitalis leaves the insoluble but active digitoxin and digitalin would be lost in filtration, but that they are held in such fine suspension by the saponin digitonin that they pass through any filter and can be absorbed from the alimentary canal.

The formation of a lather or froth is favoured by alkaline or neutral reaction, but the bubbles like those of soap are destroyed by alcohol. The saponins in general have a high molecular weight.

Chemistry.—The sapo-glucosides are mostly neutral in reaction though some few are acid. They are almost all soluble in water, the acid saponins in presence of alkali.

Solubility.—Almost without exception they are soluble in warm 90 per cent. methyl or ethyl alcohol, but all are insoluble in ether, chloroform, benzol, acetone or carbon disulphide, and the greater number also in cold absolute alcohol. They contain no nitrogen.

Hydrolysis.—Heated with dilute mineral acids the saponins yield one or more sugars (glucose, galactose, fructose, arabinose, rhamnose have been found), and a single saponin may contain more than one sugar, but saponins do not reduce Fehling's solution until they have been hydrolysed. After the separation of the sugar by hydrolysis from the saponin molecule an insoluble body called sapogenin is left with which a resin-like substance may be associated. Sometimes hydrolysis yields a uniform sapogenin, and this is then optically inactive, but often after the first hydrolysis there remains, instead of a simple sapogenin, a so-called primary sapogenin or intermediary substance still containing sugar, a glucoside, pentoside or the like, which only yields up its sugar on the employment of more intense methods. The final product is then called an end-sapogenin. The following diagram from Winterstein (9) shows what may occur.

Saponin → Resin; primary intermediary body or Isapogenin; Glucose

primary intermediary body → Crystalline sapogenin or amorphous sapogenin; Pentose

Action of Enzymes.—Kobert (6, p. 40) investigated the action of animal enzymes obtained from spiders, scorpions, flies, cantharides, cockchafers, etc., and found that they have little or no power to split up saponins. Winterstein (9) did not find that Taka-diastase, diastase or invertine had more than a minimal action on saponin, only a very small amount of sugar resulted. Halberkann (10) says that assamin is not acted upon by emulsin or pepsin. In fact at present no vegetable ferment is known to act upon saponins so as to set sugar free.

Ultra-violet Rays.—Under the influence of ultra-violet rays on saponin a reducing sugar appears in the solution, but no insoluble sapogenin is formed as is the case when hydrolysis

is accomplished by means of mineral acids (Solacolu (11)).

Concentrated saponin solutions treated with barium hydrate yield a precipitate which consists of a saponin-barium compound not of the nature of a salt (Stütz (12)), and on removal of the barium the sapo-glucoside is obtained free from colouring matter, but as its activity is materially reduced it has obviously suffered some chemical change.

Sapo-glucosides all combine with lead, and lead may be used to separate acid from neutral saponins. (See under Preparation, p. 734.) In each case the lead compound can be decomposed by H_2S and the neutral or acid saponin extracted with hot alcohol and precipitated with ether. The saponins thus obtained have not lost in activity.

It is probable that in many plants saponins exist in combination with calcium, for the ash of saponins obtained by the alcohol method mostly contains calcium.

Permanganate of potassium is reduced in solution by saponins.

With concentrated sulphuric acid saponins first turn red, then violet, sometimes with fluorescence. Warmed with Nessler's reagent saponin solutions turn first yellow, then grey (Vanwakas (13)).

Many saponins form with copper a beautiful emerald-green jelly (Halberkann *l. c.*).

Boiled with sodium-potassium or barium-hydrate the saponins lose a fatty acid group and at the same time much of their activity.

Substitution Products.—The saponins appear to possess a certain number of alcoholic hydroxyl groups which can be replaced by acetyl (Stütz *l. c.*) or benzoyl (v. Schülz (14)) groups. Wentrup (15) obtained an ester by heating saponin from Gypsophila with sodium acetate and acetic acid. Six hydroxyl groups were displaced and Wentrup gives the formula for the new body as $C_{18}H_{22}O_{10}(CH_3CO)_6$, with a molecular weight of 656. With the same sapo-glucoside Wentrup (*l. c.* p. 34) obtained a benzoyl ester with the formula $C_{18}H_{25}O_{10}$-(C_6H_5CO) and a molecular weight of 716 and a methyl-saponin $C_{18}H_{27}O_{10}(CH_3)$.

Flückiger (5) was the first who attempted to introduce an empirical formula for the saponins. He suggested that they are members of an homologous series, $C_nH_{2n-10}O_{18}$; however, only a few saponins have been found to fit this. Kobert (3, p. 147), as the result of a large number of investigations, proposes for one group the formula $C_nH_{2n-8}O_{10}$, and he gives a list of thirty-four members beginning with Entada-saponin $(C_{15}H_{22}O_{10})_3$, and ending with acid Randia-saponin, $C_{30}H_{52}O_{10}$, which belong to this series. There are also other groups for which tentative formulas have been suggested, for instance $C_nH_{2n-16}O_{28}$, which includes digitonin, $C_{55}H_{94}O_{28}$.

Reaction with Cholesterins and Phytosterins.—Of considerable interest are further the combinations of saponin with cholesterin, the saponin-cholesterides. The action of cholesterin in inhibiting the hæmolytic activity of saponins having been demonstrated (Ransom (16)), it was next shown (Hausmann (17)) that the occupation of the hydroxyl group in cholesterin prevents the reaction with saponin, *e. g.* cholesterylacetate or cholesterylbenzoate when added to saponin solutions do not hinder hæmolysis. Hausmann also found that various phytosterins prevent hæmolysis just as cholesterin does. Windaus (18) prepared pure and analysed a cholesteride of the saponin digitonin giving the compound the formula $C_{83}H_{140}O_{29}$; this saponin-cholesteride has no hæmolytic action and is not poisonous to frogs' hearts. Windaus prepared similar non-poisonous bodies by the combination of phytosterin, stigmasterin, β-cholestanol and koprosterin respectively with saponins, and he suggests that the reaction may be used both to purify saponins and to detect the presence of cholesterin. From digitonin-cholesteride Windaus obtained digitonin in crystalline form with the formula $C_{55}H_{94}O_{28} = C_nH_{2n-16}O_{28}$, and various other saponins are known which conform to this formula.

Dioscin, a sapo-glucoside from the root of Dioscorea Tokoro Makino, a plant used by the Japanese for narcotising fish, has been obtained crystalline (Honda (19)), and is a powerful hæmolytic; according to Yagi (20) it forms a crystalline compound with cholesterin, dioscin-cholesteride, which has no hæmolytic action. It consists of two molecules of cholesterin and three molecules of dioscin. Yagi suggests that those saponins which have only feeble hæmolytic powers have less affinity for cholesterin and dissociate from it more readily than do the stronger hæmolytics.

Lummerzhein (21) has recently described a cyclamin-cholesteride which dissociates with great readiness. Halberkann (*l. c.*) found that assamin-cholesteride is a non-poisonous and very insoluble compound. Madsen and Noguchi (22) also do not consider that saponin undergoes any serious chemical change in the union with cholesterin, for they were able, like other investigators, to regain sugar and saponin readily from the cholesteride. In correspondence with other observers Halberkann (*l. c.*) finds that the introduction of acetyl into a saponin molecule (assamin) destroys the hæmolytic power of the saponin and that barium-hydrate does the same. Kobert had already noted this for quillaia-saponin. Windaus' researches prove that both animal and vegetable cholesterins

combine with saponins to form non-poisonous cholesterides. The union takes place readily in alcoholic solutions.

Frænkel and Kirschbaum (23) claim to have precipitated preparations of digitalis with cholesterin and to have obtained by this means a digitalis preparation free from the saponin digitonin.

The digitonin-cholesteride is to be regarded as a chemical entity and not as an adsorption product; there is no great alteration in the digitonin molecule, for so soon as the cholesterin is removed the toxity of the saponin is restored.

Sieburg (24) has found for an acid saponin from strophanthus seeds the formula $C_{21}H_{34}O_{10}$ which corresponds to Kobert's $C_nH_{2n-8}O_{10}$, and helleborein has the same constitution (Sieburg (25)).

The above facts show that the saponins are more or less nearly related chemically to each other, and that a large number of them are included under Kobert's formula $C_nH_{2n-8}O_{10}$. For the present, however, there is no very evident connection between their toxicity and their position in such a series.

The sapogenins obtained by hydrolysis of sapo-glucosides are to be regarded as acids.

Sapogenins.—They turn congo-red blue and form salts with alkalis, some of which are crystalline. They are mostly very insoluble in water. On decomposition sapogenins have been found to yield formic, acetic and butyric acids. As has been noted above, the primary sapogenins are, properly speaking, sapo-glucosides and act as such. Laube (26) found that primary sapogenin from saponalbin still caused hæmolysis, but not nearly so well as saponalbin itself. If the saponin molecule is hydrolysed till all sugar is removed there remains the end-sapogenin. The end-sapogenins fall into two groups of which the one have the formula $C_nH_{2n-6}O_2$ and are called sapogenols, the other group have the formula $C_nH_{2n-6}O_3$ and are called oxysapogenols (Kobert).

On account of their insolubility the hæmolytic power of the sapogenins is difficult to test, but it is generally less than that of the corresponding sapo-glucoside.

Pharmacology.—The sapo-glucosides are all in various degrees protoplasmic poisons. Excised portions of nervous or muscular tissue exposed to their action undergo more or less change of structure, the cells of the liver, kidney, brain etc., often quickly lose all their characteristic appearances, the red blood corpuscles are altered and the blood is laked. However, red corpuscles, liver and other cells after hardening with Hayem's solution or formaldehyde resist the action of saponins, and $CaCl_2$ or $MgCl_2$ also delay hæmolysis.

Fish are very susceptible to the poisonous action of saponins, and hence these bodies have been used from ancient times to facilitate the catching of fish. Tadpoles are also very easily poisoned. It is curious that seeds containing saponins do not appear to be protected against the attacks of insects (Halberkann, assamin). On account of their destructive action on unprotected protoplasm certain saponins have been used as anthelmintics, *e. g.* Albizzia anthelmintica (Mimosa).

Local Application.—Applied to mucous membranes the saponins are irritating, often intensely so, causing respectively coughing, sneezing, salivation, vomiting and diarrhœa. Subcutaneously administered they are apt to cause extreme irritation and even aseptic suppuration.

Hæmolysis.—The power of hæmolysis is possessed by all saponins though in very varying degree; it is probably the most delicate test which we know for their detection in weak solution (Rühle (27), Rusconi (28), Sormani (29), Behre (30)). However, the erythrocytes are by no means the most susceptible of the body cells to the action of saponin, and if by any means saponins obtain an entrance into the organism, death may, and often does, take place without hæmoglobinuria from paralysis of the central nervous system.

Hæmoglobinuria.—Doses of from 0·3–1 gr. of Merck's sapotoxin administered intravenously to rabbits did not produce hæmolysis, the minimal fatal dose caused in general neither hæmoglobinuria nor methæmoglobinuria, death was due to poisoning of the central nervous system (Isaac and Mœckel (31)); in order to produce hæmolysis in the bodies of rabbits much larger doses than the above had to be given. On the other hand hæmoglobinuria with extravasation of blood into the walls of the peritoneal cavity and into the intestinal walls is frequently found, especially in more susceptible animals (dogs) after a fatal dose of saponin, and hæmoglobinuria is not uncommon after less than a fatal dose.

Toxicology.—It has been said above that saponins, with the exception of the one from agrostemma or corncockle, are absorbed with difficulty from the intestinal tract. Brandl (32) found that very much larger doses are required to produce symptoms of poisoning if the saponin is given by the mouth than when it is administered subcutaneously or by a vein. The acid and the neutral saponins were about equally poisonous. By the mouth 0·71 gr. pro. kg. killed a pigeon in about twelve hours. The first symptoms were salivation, vomiting and diarrhœa, followed by coma and respiratory death; post-mortem, hæmorrhagic infiltration in the œsophagus and stomach, and hæmorrhage in the intestine were observed. Saponin from

Bassia longifolia given subcutaneously killed rats in less than an hour, causing paralysis of hind limbs and respiratory death; post-mortem, blood-stained serum in the peritoneum and hæmorrhages in the intestinal walls were found. Given by the mouth it had no effect at all (Moore, *l. c.*). Brandl was unable to find saponin in the fæces, and considers that saponin is destroyed in the intestinal canal of pigeons and fowls. On the other hand, he found some sapogenin in the fæces of dogs poisoned with saponin, which seems to show that saponin may be in part decomposed in the intestine, although neither pepsin-hydrochloric acid, trypsin, diastase nor ptyalin act upon it *in vitro*. Administered to pigs by the mouth (0·54 mg. pro. kg.) saponin caused acute gastro-enteritis and toxic hæmolysis. The experiments are of importance in view of the fact that saponin has been added to lemonade and such-like drinks to produce a more permanent frothing. Both Kobert and Brandl are of opinion that the effect of saponin (agrostemma) by the mouth depends to a large extent upon the condition of the alimentary tract at the time the saponin is taken. Moreover, Lehmann and Mori (33) have shown that human beings are vastly more susceptible to saponin (agrostemma) than are the domestic animals.

Hæmolysis *in vitro*.—The various saponins differ greatly in their hæmolytic powers, *e. g.* cyclamin parillin and digitonin are active in 1 in 100,000 dilution, whereas guaiacum and trevesia saponins will not bear dilution over 1 in 10 (Kobert (6, p. 18)).

The blood of different animals varies in its resistance to saponins, but the washed red cells themselves do not differ greatly in this respect. Laube, however, with a minimum of washing found distinct differences. The hæmolysis appears to be due to the action of saponins upon the lipoid bodies of the stroma. The formation of saponin-cholesterides has already been alluded to. Ransom (*l. c.*) showed that cholesterin added to saponin solutions prevents hæmolysis, and that serum extracted with ether is deprived of the protective power which it otherwise exerts.

Reaction with Lecithins.—Kobert (6, p. 48) found that saponins also enter into combination with lecithins and is of opinion that the lecithin contained in the stroma of the red cells is dissolved by saponin, thus helping the occurrence of hæmolysis. The saponin-cholesterides are, however, not hæmolytic, whereas the saponin lecithin compounds are, *i.e.* cholesterin protects the cells against the action of saponin, lecithin does not (Ransom (16), Noguchi (34)).

Resistance of red blood cells in Disease.—An examination (Heuberger (35)) of the resistance to saponin offered by human red blood corpuscles from persons suffering from various diseases did not show any marked differences, when the number of red cells in the unit of volume was taken into account.

Abderhalden and Frey (36) investigated the action of saponin upon the blood of a horse suffering from pernicious anæmia, and found (1) that larger amounts of saponin were needed to produce hæmolysis than with blood of a normal horse; (2) the washed red blood cells were about as susceptible as those of a normal horse; (3) the serum of the anæmic horse inhibited the action of saponin much more strongly than did the serum from the control horse.

Experimental Chronic Poisoning.—In more chronic poisoning by saponins distinct action upon the blood elements and upon the blood-forming organs have been noticed. Isaac and Mœckel (*l. c.*) found reduction in the number of red cells, diminution of hæmoglobin, and a considerable number of megaloblasts. There was no marked leucocytosis but a large percentage of mononuclear cells with basophile protoplasm. The bone marrow showed marked degeneration and destruction of blood-forming tissue, frequently a total loss of all specific cells with marked fibrous changes and increase of fat; further myeloid changes in the liver and spleen and in the latter a great number of megaloblasts. In almost all cases there was an increase of cholesterin in the serum (Abderhalden and Frey). Pappenheim and Szécesi (37) also noted changes in the bone marrow but do not consider that saponins cause genuine anæmia.

Action on the Hæmopoietic Organs.—It appears, therefore, that saponins have a specially intense action upon the hæmatopoietic apparatus leading to cell destruction.

Heart.—All the saponins have a more or less powerful effect on the excised hearts of frogs and other cold-blooded animals. At first the systole becomes more effective and slower, but the heart tends to pass into a condition of systolic rigor (Kobert, Straub, (6 p. 54)). They appear, however, only to act thus when brought into immediate contact with the ventricle (Karaúlow (38)), and do not often cause delirium cordis (Moore (*l. c.*)). Using Straub's method, Postojeff (39) found that the addition of saponin (Merck's) in non-toxic doses to small doses of digitoxin (Merck's) very considerably increased the toxicity of the latter. Fränkel and Kirschbaum (*l. c.*) are of opinion that the stomach and intestinal irritation sometimes following the use of digitalis drugs are to be referred chiefly to the presence of the saponin group (digitonin) and only to a small extent to the digitoxin; they observed that digitalis preparations freed by means of

cholesterin from digitonin always caused frogs' hearts to die in systole, whereas the untreated drug often stopped the heart in diastole.

Striped Muscle.—The saponins have a distinct action on striped muscle, changing more or less completely its microscopical appearance. They appear to act injuriously in about the same concentration as that in which they produce hæmolysis (E. Overton (40)). The end-sapogenins, especially after being dried, are very insoluble; they still have, however, some hæmolytic power. Laube (*l. c.*), using end-sapogenin of saponalbin (from radix saponari alba) and rabbit's red corpuscles, found as maximum dilution for saponalbin 1 in 43,000, for the primary sapogenin 1 in 6000 and for the end-sapogenin 1 in 600. He also noted that the end-sapogenin in stronger solution causes agglutination against which the serum protects. On the other hand assamin-sapogenin was found more powerfully hæmolytic than assamin.

Reaction with Serum and Rennet.—The saponins have a very remarkable effect upon the action of serum in inhibiting the activity of rennet (Jahnson-Blohm (41)). The inhibitory action of serum is almost entirely prevented by the previous addition of saponin to serum, and this reaction takes place very quickly. On the rennet itself saponin has no effect at all. Even after rennet and serum have been mixed for some time the addition of saponin sets some rennet free. On the other hand, saponin has no effect in diminishing the inhibitory action of rennet-immune serum on rennet; on the contrary, rather increases it. Charcoal in suspension added to rennet delays coagulation, but if the charcoal suspension is first treated with saponin before being added to rennet there is no delay in the action of the latter. If the charcoal and rennet are first brought together and saponin added afterwards, more or less of the rennet is set free. Charcoal holds saponin so firmly that the latter cannot be washed out with water. The adsorption of trypsin by charcoal can also be prevented if the charcoal is first treated with saponin. It appears, moreover, that though saponin has no action on rennet, yet it activates zymogen.

Therapeutics.—The therapeutic uses of saponins are quite limited; they have been used as expectorants in consequence of their irritant action on the stomach, causing more or less nausea, but other drugs are more efficient and less dangerous. They are also sometimes used to emulsify oils and to make fine suspensions. It will be seen from what has been said above concerning their poisonous activity that their use in gingerbeer, lemonade and similar liquids ought not to be allowed.

Preparations

Quillaiæ Cortex (B.P.), Quillaja (U.S.P). Panama bark, Soap bark, the inner bark of Quillaia Saponaria.

Extractum Quillaiæ Liquidum (B.P.C.). Used diluted externally.

Fluidextractum Quillajæ (U.S.P.). 3 min. (2 dl.).

Tinctura Quillaiæ (B.P.). ½–1 fl. dr. (2–4 ml.).

Tinctura Quillajæ (U.S.P.). ½–1 fl. dr. (2–4 ml.).

Sarsæ Radix (B.P., 1898). Sarsaparilla, the root of Smilax ornata.

Decoctum Sarsæ (B.P., 1885). 2–10 oz. (60–300 ml.).

Decoctum Sarsæ Compositum (B.P., 1885). 2–10 fl. oz.

Extractum Sarsæ Liquidum (B.P., 1898). 2–4 fl. dr.

Liquor Sarsæ Compositus Concentratus (B.P., 1898). 2–8 fl. dr. (8–30 ml.).

Sarsaparilla (U.S.P.). The root of Smilax medica and other species.

Fluidextractum Sarsaparillæ (U.S.P.). 30 min. (2 ml.).

Fluidextractum Sarsaparillæ Compositum (U.S.P.). 30 min. (2 ml.).

Syrupus Sarsaparillæ Compositus 4 fl. dr. (16 m.).

Senegæ Radix (B.P.). The root of Polygala senega.

Infusum Senegæ (B.P.). ½–1 fl. oz. (15–30 ml.).

Infusum Senegæ Concentratum (B.P.C.). ½–1 fl. dr.

Liquor Senegæ Concentratus. ½–1 fl. dr.

Tinctura Senegæ (B.P.). ½–1 fl. dr. (2–4 ml.).

Senega (U.S.P.). The root of Polygala senega.

Fluidextractum Senegæ (U.S.P.). 15 min. (1 ml.).

Syrupus Senegæ (U.S.P.). 1 fl. dr. (4 ml.).

The preparations of Sarsaparilla are incompatible with alkalies.

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F. R.

IPECACUANHA AND EMETINE

Ipecacuanhæ radix, commonly known as Ipecacuanha, or Ipecac, is the dried root of Psychotria (Cephaelis) Ipecacuanha, a plant indigenous to Brazil, but cultivated also in the East Indies. The so-called "Cartagena Ipecacuanha," obtained from an unidentified species of Psychotria growing in Colombia, is also official. Ipecacuanha has long had an empirical application as an emetic and expectorant, and a reputation, with an equally empirical basis, in the treatment of tropical or amœbic dysentery. For a good many years it has been possible to attribute the emetic and expectorant properties of the drug to the alkaloids which it contains; but a similar rationalisation of its use in amœbic dysentery is one of the most recent, and not the least interesting and important, of the achievements of experimental pharmacology and therapeutics. It is but a few years since the opinion was widely expressed and adopted that ipecacuanha owed its value in dysentery to non-alkaloidal constituents, and a preparation of the drug, freed from the supposedly undesirable alkaloids ("deemetinised" ipecacuanha), was freely prescribed in such cases. It was shown, however, by Vedder, and has been confirmed by a number of subsequent workers, that the chief alkaloid of ipecacuanha, emetine, had a lethal effect on amœbæ in high dilutions, while extracts of the drug deprived of alkaloids were practically free from such action. Leonard Rogers first applied this observation in clinical experiment with such success that the use of emetine in amœbic dysentery bids fair to rival that of quinine in malaria, both in the promptitude and the specificity of its action.

Active Principles.—Three alkaloids have up to the present been discovered in Ipecacuanha, and to these are attributable all its known therapeutic and toxic effects. Of the total alkaloidal content three-quarters consists of Emetine, $C_{29}H_{40}O_4N_2$, the remainder being chiefly Cephaeline, $C_{28}H_{38}O_4N_2$. It will be seen that emetine differs from cephaeline by CH_2, a hydrogen atom being replaced by a CH_3 group; in other words, it is methyl-cephaeline. The third alkaloid, Psychotrine, no formula for which has yet been published, occurs only in very small proportion. The total alkaloidal content of good specimens of the drug is about 2 per cent. In the Cartagena Ipecacuanha cephaeline is said to constitute a larger proportion of the alkaloid than emetine.

The hydrochloride of emetine, a soluble crystalline salt, is the one used in therapeutics.

Action.—The alkaloids possess, and impart to the drug, a marked local irritant action, which, however, varies considerably with different individuals. This causes an inflammatory reaction of any mucous membrane to which the drug is applied, or of the skin in sensitive subjects. The most familiar effect of this irritant action is the vomiting which is promptly produced when a sufficient dose of the drug or of its alkaloids is given by the mouth. Like other gastric irritants, Ipecacuanha in smaller doses by the mouth produces an increase of tracheal and bronchial secretion, and is therefore used as an expectorant when secretion is scanty. Whether this increased secretion from the respiratory passages, and the increased flow of saliva and of sweat which the drug also causes, are to be attributed entirely to the reflex effects of gastric irritation, is a question which seems to need further investigation. The point cannot be immediately settled by the

effect of hypodermic injections of the alkaloids; for they are rapidly excreted by the mucous membrane of the stomach and bowel, and in the process cause nausea and vomiting, although less readily than when given by the mouth. So easy is it, indeed, to produce vomiting by parenteral administration of the alkaloids that some observers have supposed that they have a direct action on the vomiting centre in the medulla oblongata comparable to that of apomorphine; but the evidence is, on the whole, against such an action. For emetine or cephaeline, when given by the mouth, produces vomiting more promptly, and in smaller doses, than when injected under the skin. Since, with toxic doses given hypodermically, the inflammatory reaction of the gastric mucous membrane bears witness to the local action on that structure, direct action on the medullary centre is a superfluous assumption until more direct evidence can be adduced in its favour.

The fact that by hypodermic administration a dose can be given, without producing vomiting, which would be inevitably emetic when given by the mouth, has recently acquired considerable practical importance, and the effects of the two modes of action may with advantage be contrasted. When a large dose of emetine is given by the mouth symptoms of nausea soon make their appearance, with the usual accompaniments of salivation, perspiration and depression, and presently the whole dose is vomited and removed from the system, practically none being absorbed. When a toxic dose is given hypodermically to a dog or cat, after an interval of twenty to thirty minutes, purgation and vomiting occur, with the usual accompaniments of salivation, etc. The fact that purgation appears as soon as vomiting indicates that the alkaloid has affected the large bowel as well as the stomach. If the dose has been a small one the effects pass off and the animal regains its normal condition. With larger doses the attempts to vomit and defæcate continue when nothing but mucus can be voided, and this may become tinged with blood. A condition of collapse supervenes, the heart becomes progressively weaker, and eventually fails. If the symptoms have been protracted, so that death occurs only after an interval of a day or so, an intense congestion of the mucous membrane of the stomach and intestine is found post-mortem, which may have progressed to ulceration. The effect appears to be most intense in the stomach on the one hand, and the colon on the other. Possibly this indicates a predominant elimination of the alkaloid in these situations. When emetine or cephaeline is injected intravenously the most prominent effect is depression of the heart's action, which, if the dose is sufficiently large, causes death of the animal before other symptoms appear. A similar rapid death from cardiac failure may result from massive hypodermic injections.

The point of chief practical importance is that emetine, given hypodermically, is excreted not only by the stomach, but by the intestine as well, so that a dose which would certainly produce vomiting by direct action, if given by the mouth, may be given hypodermically and, being spread over a wider area of alimentary mucous membrane, cause no untoward symptoms. The fact that some of the alkaloid is excreted by the mucous membrane of the colon probably has an important bearing on its value in amœbic dysentery. It cannot be suggested, however, that its local concentration in this manner is necessary to its efficacy as an amœbicide, since numerous cases are now on record in which injections of emetine have caused a rapid disappearance of liver abscesses due to amœbic infection.

Of the three alkaloids of Ipecacuanha emetine is not only the most abundant, but, therapeutically, the most important. Cephaeline has an action of the same general type, and is said to be equal to emetine in amœbicidal power; but it is many times more toxic, both its minimal lethal dose and its minimal emetic dose being much smaller than those of emetine. Psychotrine, on the other hand, has a much smaller toxicity than emetine. Its amœbicidal action has not yet been investigated; but it occurs in Ipecacuanha in such comparatively minute proportions that it can be safely assumed that it plays, at any rate, no considerable part in the action of the drug.

The effect of emetine on amœbæ appears to be a highly specific one. There is no evidence of its producing any effect on ciliate infusoria, for example, in the high dilutions in which alone the body can tolerate it in circulation. On the other hand its amœbicidal action appears not to be limited to the entamœba histolytica, or even to the parasitic genus entamœba. It is certain that some of the experiments published, in which the lethal effect of very high dilutions of emetine on cultures of amœbæ has been recorded, were made on the free-living, non-parasitic amœbæ, no entamœba having as yet been grown with certainty in artificial culture. Even if each of the various pathogenic entamœbæ which have been described should ultimately, and contrary to the present tendency of evidence, establish its claim to be a separate species, there is no reason as yet to expect that any of them will prove to be especially resistant to emetine.

Therapeutic Uses.—It is probable that the prescription of Ipecacuanha and its galenical preparations will in future be confined to its

use as an emetic, expectorant and diaphoretic. Since these actions depend largely, if not entirely, on its gastric irritant action, administration by the mouth is alone admissible. For the same reason, the drug and its preparations, containing the more powerfully emetic cephaeline, are to be preferred to the salts of emetine for these purposes. Its value as an expectorant is obviously limited to those cases in which the bronchial secretion is deficient. The most commonly used preparation, both as an emetic (especially in children) and in smaller doses as an expectorant, is the Vinum Ipecacuanhæ. As a diaphoretic in incipient respiratory catarrh the well-known Dover's powder, in which Ipecacuanha is associated with opium, is commonly used. This powder, made into a pill, with squill in addition, is also a favourite expectorant.

In the treatment of amœbic dysentery it was till recently the custom to administer powdered ipecacuanha in large doses, using morphine, sinapisms, ice, posture, or any device which could be supposed to have a restraining action on the vomiting reflex. This method is rapidly being replaced by the administration of the salts of pure emetine. Hypodermic administration is mostly used, the dose being gradually increased from $\frac{1}{3}$ up to 1 gr. Some observers have recommended the administration of the alkaloidal salt by the mouth, in tablets coated with some substance such as keratin, which resists gastric, but not pancreatic, digestion. This would seem to be a reasonable practice, if it be remembered that the success of the procedure depends on the rapid passage of the tablet from the stomach. If it remains there, sufficient of its contents may pass through the coating by diffusion to produce vomiting and render the administration ineffective. It would seem reasonable, therefore, to give, at the same time as the dose, a small and quickly digested meal, such as a draught of milk or a bowl of gruel, on a previously empty stomach.

Neither ipecacuanha nor emetine appears to have any value in dysentery of purely bacterial origin. It is, perhaps, desirable to allude to another empirical application of ipecacuanha, the reputation of which seems to have been locally restricted. It is stated that the drug has a marked effect on anthrax if applied locally to the pustule. In this instance again, the de-emetinised drug has been alleged to give equally good effects. In view of the recent evidence as to the mode of action of the drug in amœbic dysentery it seems desirable that this reputed action on anthrax should be experimentally investigated, especially as the anthrax bacillus seems to be peculiarly susceptible to the action of certain drugs (*e.g.* salvarsan) of which the characteristic effect is antiprotozoal.

Materia Medica and Preparations

Ipecacuanhæ Radix (B.P., U.S.P.).
Dose: Expectorant $\frac{1}{2}$–2 gr. (3–12 cg.). Emetic 15–30 gr. (1–2 g.).

Extractum Ipecacuanha Liquidum (B.P.).
Dose: Expectorant $\frac{1}{2}$–2 min. (3–12 cl.). Emetic 15–20 min. (10–12 dl.).

Fluidextractum Ipecacuanhæ (U.S.P.).
Average dose: Expectorant 1 min. (5 cl.). Emetic 15 min. (1 ml.).

Pilula Ipecacuanhæ cum Scilla (B.P.).
Dose: 4–8 gr. (25–50 cg.).

Pilula Ipecacuanhæ cum Urginea (B.P.).
Dose: 4–8 gr. (25–50 cg.).

Pulvis Ipecacuanhæ Compositus (B.P.).
Dose: 5–15 gr. (3–10 dg.). (Dover's powder.)

Pulvis Ipecacuanhæ et Opii (U.S.P.).
Average dose: $7\frac{1}{2}$ gr. (5 dg.).

Tinctura Ipecacuanhæ et Opii. (U.S.P.).
Average dose: 8 min. (5 dl.).

Trochiscus Ipecacuanhæ (B.P.).
Dose: 1–3.—$\frac{1}{4}$ gr. (15 mg.) Ipecac. in each.

Vinum Ipecacuanhæ (B.P., U.S.P.).
Average dose: Expectorant 10–30 min. (6–18 dl.). Emetic 4–6 fl. dr. (16–24 ml.).

Syrupus Ipecacuanhæ (U.S.P.).
Average dose: Expectorant 15 min. (1 ml.). Emetic 4 fl. dr. (16 ml.).

Emetinæ Hydrochloridum (B.P.C.).
Dose: (hypodermically) $\frac{1}{3}$–1 gr. (2–6 cg.). Also by the mouth in capsules resistant to gastric digestion. H. H. D.

ESSENTIAL OILS, BALSAMS AND STEAROPTENES

Primitive man seems to have always associated powerfulness of odour and disagreeableness of taste with potency of remedial action; and the contents of this chapter are evidence that this superstition has not as yet disappeared, even in this scientific age, amongst the world's most civilised peoples. Many odours considered pleasant by our forefathers who lived before the age of universal cleanliness are now offensive to us, and the same is true of the flavours which we appreciate; anise, caraway, and garlic are undoubtedly declining in popularity. The very source of musk would now be sufficient in itself to deter most persons from either giving or taking it.

The earliest drug collections are evidence that belief in odour and in pharmacological action went hand in hand. The earliest Egyptians used Anise, "the leg of the Ibis," and the North American Indians had a firm belief in the value of Sassafras. As commercial relations grew, the pharmacopœias of civilisation

were enriched by the drugs used by the medicine-men of the whole world. Drugs from India and the Spice Islands of the East were long employed, and the exploration of America and Africa led to numerous additions.

The drugs thus gathered together constitute a motley group; but this chapter deals mainly with those whose odours are due to the presence of an essential oil or one of its chemical congeners, resins, stearoptenes or balsams. Some few other drugs characterised by marked odours and taste which chemically do not belong to the group are considered with them for purely pharmacological reasons, and some which might be considered here are not treated of as they belong more properly in other groups and are described elsewhere, for example in the section on *Drugs acting upon the Skin*.

The *essential oils* superficially resemble the true or fixed oils in being, as a rule, lighter than water, soluble in ether, chloroform and alcohol, and very slightly soluble in water, but sufficiently so that they impart to it their characteristic flavours. They leave a greasy mark on paper which, however, as they are all volatile, disappears with greater or less rapidity. Their volatility is as a rule taken advantage of in their preparation, as they are generally obtained by distilling with steam the plants or plant-products in which they are found. Some, however, are obtained by expression and some by extraction with oil. Chemically most of the essential oils are hydrocarbons of the aromatic group, and many of them consist very largely of mixtures of various terpenes, bodies which have the general formula $C_{10}H_{16}$. Among the more important and commonly occurring terpenes are *pinene*, occurring in oil of pine, turpentine, and in the oils of thyme and of lemon; *camphene*, which is solid and occurs in camphor, ginger and valerian; *limonene*, occurring in lavender, caraway and turpentine. In many plants oxidised terpenes are found such as safrol (in sassafras) and in others hydroxylated terpenes, *e. g.* eugenol (in cloves). Oils from the plants of the Cruciferæ frequently contain sulphur and cynagen, *e. g.* oils of mustard and garlic. A few of the essential oils do not belong to the aromatic group, of these oil of mustard is a prominent example.

Terpenes in contact with the air rapidly undergo oxidation and then contain *resins*. In the process of oxidation they usually become much darker in colour or, if colourless when pure, become characteristically coloured. The resins are highly complex bodies usually acid and solid. In nature they are never found in a pure state, and indeed it is usually difficult to purify them.

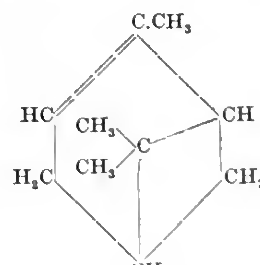
The *oleo-resins* are solutions of resins in oil or of oil in resins. The *balsams* are resins or oleoresins which contain benzoic or cinnamic acid or both or their esters. The *gum-resins* are mixtures of resins and gum; the property that distinguishes this group from the others is that owing to the gum they contain they form emulsions if thoroughly rubbed up with water. Myrrh may be cited as an example.

Many essential oils contain substances which crystallise out if the oil be cooled. These solid bodies are known as *stearoptenes* (*στέαρ* and *πτηνός*); the fluid residues as *elæoptenes* (*ἔλαιον*).

In their natural state the essential oils, oleoresins, resins and balsams contain small quantities of other bodies, phenols, aliphatic acids, ketones, etc., which in some cases play an important part in their pharmacological activities.

The Essential Oils, Oleoresins and Balsams.— In as far as the action of any of these bodies depends upon the presence of a terpene, it will conform more or less closely to a general type of which turpentine is the best known and most characteristic example. This will be first described, and in treating of the other members of the group no detailed account will be given of their general action save when they differ in an important manner from turpentine. The other members of this group are considered under various sub-heads, descriptive of the therapeutic action for which each member is most commonly employed and a general description of the pharmacology of each group is given. The drugs in each group are arranged as far as possible in the order of merit and of the frequency with which they are employed.

Oleum Terebinthinæ Rectificatum (B.P.). Oil of Turpentine). 2–10 min. (12–60 cl.); as an anthelmintic 3–4 fl. dr. (12–15 ml.). The crude oil of Pinus sylvestris, turpentine, yields on distillation with steam about 15 per cent. of the official oil. The formula of Pinene, the most important terpene it contains, is $C_{10}H_{16}$. It is readily seen



that it is chemically related to the benzenes, and this serves to suggest that it will both be volatile and toxic to living protoplasm. It is consequently an antiseptic (Bucholtz), but is more toxic to moulds than to bacteria.

Applied to the skin it penetrates rapidly,

stimulates the sensory endings, producing a sense of warmth and a dilatation of the vessels and slowly develops a typical rubefacient action.

It has a characteristic bitter pungent taste, which most persons find particularly abhorrent. When taken into the mouth it causes reflexly from the sensory endings a flow of saliva and probably of gastric juice. In the stomach small doses act as a carminative, causing a sense of warmth and probably a dilatation of the vessels and an increase in movements, and some decrease of bacterial growth. In large doses it is intensely irritating, quickly causing tissue necrosis and leading to vomiting and purging. On absorption it causes a polymorphonuclear leucocytosis, possibly because being positively chemotactic, it tends to prevent the escape of the white cells from the blood stream (Pohl).

In pharmacopœial doses it has no further observable effect, and indeed, in doses of approximately one fl. drachm, Purkinje felt only a slight depression and dulness. In larger and toxic doses it produces a transitory stimulation of the central nervous system, with some languor, dullness, sleepiness, sensory depression, loss of reflex action, and coma (Midall). Its action on the respiratory and circulatory centres consists in a primary stimulation, reflex and central, and a subsequent depression.

Small amounts are excreted unchanged by the lungs and by the skin, but for the most part it undergoes hydroxylation and is chiefly excreted by the kidneys in combination with glycuronic acid (Schmiedeberg), Fromm and Hildebrandt); small amounts may appear in the urine unaltered. Its excretion is accompanied by an increased diuresis, but in large amounts it produces such marked renal damage that the urinary flow may be decreased or stopped. It may be recalled that it causes glycuronates to appear in the urine which may lead to the reduction of Fehling's solution.

Oil of turpentine is now chiefly used as a rubefacient, but is occasionally administered as an anthelmintic, when it should be rapidly followed by a purgative. It is not uncommonly added to purgative enemata as an irritant. It has been superseded as a hæmostatic by drugs having less necrotic action, and the use of old and oxidised oil which contains some ozone as a means of treating phosphorus poisoning has been properly abandoned.

Oleum Terebinthinæ Rectificatum is prepared by redistilling the oil from lime water, as this procedure removes acids and resins. The *Linimentum Terebinthinæ* (B.P., U.S.P.) and the *Linimentum Terebinthinæ Aceticum* (B.P.), which contains glacial acetic acid and camphor, are both useful; the second is more irritant than the first and acts more rapidly. The *Emulsion* (U.S.P.) 1 fl. dr. (4 ml.) containing 9 min. of the oil and the *Confection* (B.P., 1885) are not frequently used. The *Enema* (B.P., 1885) contains about 2 per cent. of the oil: about 16 fl. oz. (480 ml.) may be given.

Expectorants and Bronchial Antiseptics.—The common inflammations of the respiratory passages pass through three stages; congestion and irritation, when the cough is frequently painful; marked mucous secretion, with less painful cough; and a catarrhal condition, when the secretion is often viscid and the cough often becomes paroxysmal in the effort to free the passages. Rationally an antiseptic treatment seems indicated at all stages, and the use of volatile antiseptics, such as the essential oils, would seem likely to meet the requirements of these cases. The difficulties in carrying out such antiseptic treatment seem to be insurmountable, and it must now be conceded that sterilisation by inhalation is impossible. The bacteria are probably always deep in the membranes, and in the second and third stages covered deeply with excretion, consequently the inhaled antiseptic fails to reach them in sufficient concentration or for a sufficient length of time. These difficulties are increased by the fact that the essential oils are all more or less irritant and can only be employed in weak concentrations, by their slight solubility in water (this may account for creosote and phenol proving more useful, as many physicians consider them to be) and by their volatility, which leads to their rapid disappearance once inhalation ceases. When administered internally such small amounts appear in the exhaled air that they probably have no antiseptic effect. It is, of course, possible that they may tend to decrease the rate of bacterial growth even if they do not produce antiseptic conditions.

Their beneficial effects when inhaled are, however, rather to be ascribed to their slight irritant action. Turpentine vapour applied dry to mucous membrane produces a decrease in secretion, and marked reddening; if, however, it be applied in solution in water it produces an increase in secretion (Rossbach). Clinical experience has also shown that if the moist vapours of these oils be inhaled, the painful congestion of the first stage of a bronchitis is often relieved. In later stages this irritant action will lead to increased rapidity of tissue growth and probably to increased activity of the cilia, which have the important function of removing secretion and débris.

Administered internally they may decrease the catarrh. This is based on the following experimental evidence. If a purulent exudate is produced by injecting "aleuronat" into the pleural cavity of rabbits, less pus will collect if at the same time some essential oil be adminis-

tered by the mouth than if they are not (Winternitz). The positive chemotactic properties of these oils apparently tends to retain the leucocytes in the blood stream (Pohl).

Terebenum (B.P.) is a liquid formed by the action of sulphuric acid on oil of turpentine and consists of a mixture of terpenes. Its more agreeable odour has led to its being substituted for turpentine in inhalations and also for internal use. *Dose:* 5–15 min. (3–10 dl.)

Oleum Pini, the oil distilled from the leaves of *Pinus pumilus*, has an agreeable odour and is certainly preferable to turpentine.

Oleum Eucalypti (B.P., U.S.P.), ½–3 min. (3–18 cl.), is distilled from the leaves of *Eucalyptus globulus* and other species. Eucalyptol (B.P.C.), 3–10 min. (2–6 dl.), chemically known as cineol, is the chief ingredient of the oil and has largely replaced it. Eucalyptus oil has an aromatic camphoraceous odour and produces a cool sensation in the mouth. It is a good antiseptic and but slightly irritant. It is in consequence very frequently employed as ingredient in nasal sprays and douches and in inhalations. It is also employed in the form of an *Ointment* as a mild antiseptic rubefacient in some types of eczema. *Eucalypti Gummi* (B.P.) and its *Trochiscus* and *Eucalyptus* and its fluid extract are little employed.

Terpin Hydrate (U.S.P.), a crystalline solid with a slight taste and no odour, seems to be admittedly inferior to the above drugs.

Oleum Cajuputi (B.P.), ½–3 min. (3–18 cl.), the oil distilled from the leaves of Melaleuca leucadendron, though it contains 60 per cent. of cineol is infrequently used. The same is true of its *Spirit* (B.P.). 5–20 min. (3–12 dl.).

Sassafras Radix. The root of Sassafras officinale and *Sassafras*, the root bark, both contain the volatile oil, *Oleum Sassafras* (U.S.P.), 3 min. (18 cl.), which consists largely of Safrol, *Safrolum* (U.S.P.), 5 min. (3 dl.). This hydroxylated terpene is excreted almost entirely unchanged by the lungs. It is, however, more toxic than many of the essential oils, and large doses if repeated produce fatty degeneration of the liver (Heffter). It has caused acute poisoning (Allright). Though formerly frequently employed, its popularity even as flavour for beverages has greatly declined.

Sub-group.—**The Balsams.**—The Pharmacopœial balsams all contain cinnamic or benzoic acids. Both these acids are very slightly irritant when applied to the skin or mucous membranes in any but the strongest solutions and volatilise slightly in water vapour. They also contain esters of these acids and varying amounts of resinous bodies. Balsam of Tolu contains a terpene. Little is known about the actions of the resins, and their most important ingredients appear to be the acids and their esters.

Cinnamic Acid has no marked pharmacological effect save that when absorbed it increases the number of leucocytes in the blood stream and the output of uric acid. This, however, may be secondary to the leucocytosis.

Benzoic Acid (B.P.) is an active antiseptic. It also produces a leucocytosis. It is excreted in combination with glycocoll as hippuric acid. Traces of benzoic acid have been found in the saliva of dogs, but not in that of man (Cushny).

Benzoinum (B.P.) is obtained from Styrax benzoin. The *Compound Tincture* (B.P.) and the *Tincture* (U.S.P.) are both used as mild stimulants to promote the healing of slight skin wounds. Poured on the surface of hot water, they give off pleasant aromatic fumes, and are frequently thus employed as inhalations in bronchitis.

Balsamum Tolutanum (B.P., U.S.P.), 5–15 gr. (3–10 dg.), is obtained from the trunk of Myroxylon toluifera; the *Tincture* (B.P.) is sometimes used in inhalations and the *Syrup* (B.P.) is frequently employed to indicate that a mixture is intended to have an expectorant action. The balsam is sometimes employed by dermatologists as a mild antiseptic.

Balsamum Peruvianum (B.P.), 5–15 gr., is also employed as a mild antiseptic, especially for scabies.

Styrax Præparatus (Storax) is rarely used.

Editorial Note.—*Grindelia* (B.P., U.S.P.), the gum plant, is coated with an oleo-resin, and contains a resin to which its action is due. It is recommended for asthma, whooping-cough, laryngeal spasm and bronchitis. The preparations are the *Extract* made with alcohol, of which the dose is 2–3 gr. in a pill with lycopodium thrice daily, and the *Liquid Extract* (B.P., U.S.P.), of which the dose is 10–20 min. (6-12 dl.) for a paroxysm of asthma, repeated every half hour or hour.

Guaiacum Resin (B.P., U.S.P.), 5–15 gr. (3–10 dg.), contains chiefly guaiaconic acid. The dried wood from which it is prepared is also official. Guaiacum is recommended for chronic rheumatism, rheumatoid arthritis, lumbago and sore throat. It enters into the composition of the Chelsea Pensioners' electuary (see *Preparations of Sulphur*), which is now frequently also put up in tablets containing 3 gr. each of guaiacum resin and sulphur. Other preparations are—

Mistura Guaiaci (B.P.).
Dose: ½ – 1 fl. oz. (15–30 ml.).
Tinctura Guaiaci Ammoniata (B.P.U., S.P.).
Dose: ½ – 1 fl. dr. (2–4 ml.).
Tinctura Guaiaci (U.S.P.).
Dose: 1 fl. dr. (4 ml.).

I.—Urinary Antiseptics and Stimulants to the Mucous Membrane of the Urinary Tract

(See also article on Urinary Antiseptics in General.)

The urinary tract may be reached readily by antiseptics excreted by the kidneys; but

here, as in the bronchi, sterilisation is practically impossible, owing to the bacteria being so deeply lodged, not only in the folds of the mucosa, but in the membrane itself. Certain conditions of absorption and excretion must also be fulfilled, if any drug is to be advantageously employed for this purpose. Absorption, or at all events excretion of the drug must not be too rapid, as otherwise renal damage will be caused in the process. The presence of protein and of casts in the urine is evidence of such a deleterious effect, but the recent experimental pathology of the kidney has shown clearly that recovery from mild types of tubular degeneration is rapid and complete. Too much alarm should not be felt if a temporary albuminuria occurs. Secondly, most antiseptic drugs undergo chemical changes and are excreted as compounds in which they are not active antiseptics. To exert such an action drugs should, then, either be excreted unchanged or in such a form as to retain their action, or as such that they will readily break down under the conditions of acidity or alkalinity present in the urine. Thirdly, in their antiseptic form they should not be so irritant as to produce pain or painful reflexes. These conditions are hard to fulfil, yet seem to be so in part by the group of essential oils and oleoresins, of which santal, copaiba and cubebs are the chief members. These are excreted in part unchanged, but chiefly as glycuronates, and as acid resinous bodies (Quincke, Karo). Save in large doses they irritate the kidney only slightly. They seem to be excreted slowly; copaiba appears in the urine within a few hours after taking it, but if taken for some days does not completely disappear for four or five days after the last dose (Quincke). The glycuronates and resins have but slight antiseptic action. The former break down in acid urine, but they are irritant, especially to inflamed mucous membranes. To avoid the pain thus caused, they are rarely given in the acute stages of an inflammation. The acid resins precipitate protein and may have a beneficial astringent action (Vieth).

Their activity in clearing up a chronic catarrhal inflammation may perhaps be best explained, not as an antiseptic action, but rather as due to their property of decreasing the number of leucocytes in an inflammatory exudate, prior to their excretion (Winternitz), and secondly, to their slight irritative action after excretion, which tends to promote the growth of healthy tissue. Clinical experience has shown that their greatest field of usefulness is in the chronic catarrh of the lower urinary passages due to infection by the gonococcus (gleet).

Oleum Santali (B.P., U.S.P.). Oil of Sandalwood. 5–30 min. (3–18 dl.). The oil distilled from the wood of Santalum album contains santalol, an hydroxylated terpene. It is not so apt to cause indigestion nor erythemata as cubebs and copaiba. It is best administered in capsules; but as its taste is spicy and pungent, it may be given as an emulsion, or in a mixture, as in the following preparations: Liquor Santali Compositus (B.P.C.), 1–2 fl. dr., an alcoholic solution, containing cinnamon, buchu, and cubebs, or Liquor Copaibæ et Olei Santali (B.P.C.), 1–2 fl. dr., or Liquor Copaibæ et Buchu et Cubebæ cum Olei Santali (B.P.C.), 1–2 fl. dr. An objection to these complex mixtures is, that if an erythema or indigestion occurs, further experimentation is necessary to determine which ingredient is at fault.

Copaiba (B.P., U.S.P.). ½–1 fl. dr. (2–4 ml.). The oleoresin from the trunk of Copaifera Lansdorfii, and Oleum Copaibæ 5–20 min. (3–12 dl.), a purified oil, are more apt to cause indigestion and produce erythemata than santal. The oil is usually given in capsules, as its taste is persistent, acrid and bitter, though it may be given in an emulsion, as in the Mistura Copaibæ (B.P.C.), or in alkaline solution as in the Liquor Copaibæ et Olei Santali.

Cubebæ Fructus (B.P., U.S.P.). 30–60 gr. (2–4 g.). The dried unripe fruits of Piper Cubebæ, contains Oleum Cubebæ, 5–20 min. (3–12 dl.). The oil is most commonly employed, the fruits and the tincture or fluid extract much less commonly. Secondary unwished-for effects seem even more common than with copaiba, and certainly more so than with santal. It is sometimes used as an inhalation in bronchitis and more rarely as the lozenge in pharyngitis.

Drugs Irritant to the Kidney.—The following drugs are especially irritant to the kidney, producing not only diuresis but also degeneration. They also irritate the intestinal canal, causing congestion and purgation. Their employment leads further to uterine congestion. They have been employed as emmenagogues, and all too frequently to produce abortion. Their sale should be prohibited, as they have no proper therapeutic use. *Oleum Juniperi* (B.P.), ½–3 min.; *Spiritus Juniperi*, 20–60 min.; *Tanacetum* (Tansy); *Herba and Oleum Pulegii* (Pennyroyal); *Sabina*; *Oleum Sabinæ*; (Savin).

Buchu Folia (B.P.). The leaves of Barosma betulina contain an oil and a bitter; their *Infusion* and *Tincture* are still employed as flavours in a diuretic mixture.

II.—Carminatives and Flavours

The work of Pawlow and his pupils have made us familiar with the dietetic value of the pleasant taste and smell of food; and has confirmed the experience of mankind. The bitter tonic or cocktail before meals may be

paralleled by the spiced cup or liqueur after them. Cannon has taught us that the production of hunger pains and of appetite is due to the increase of tone in the stomach walls, which must precede its functional movements. The pungent spicy flavour so characteristic of some plants and their products, and such as is possessed by many essential oils, produces the feeling of hunger and a reflex flow of saliva and gastric juice. On reaching the stomach a feeling of warmth and well-being is produced, with a dilatation of the vessels of the viscus, and doubtless an increase in its tone and in its movements, as a prompt eructation of any gas that is contained in the stomach frequently follows their use. Absorption of the products of digestion is promoted (Brandl), possibly as a consequence of the increased blood supply, possibly by some specific action as was shown for bitters by Jodlbauer. The essential oils are all antiseptic; but it is difficult to estimate whether this action is of much value in decreasing fermentation or not. Drugs with these actions are termed *Carminatives.* A carminative on reaching the intestine acts in a similar manner, dilating the blood-vessels, increasing the absorption of food-stuffs (Scazoni and Farnsteiner) and of gas, and probably increasing and making more regular the intestinal movements. Long clinical experience has shown that they are useful ingredients in laxative pills. The alcoholic form in which they are so usually administered undoubtedly contributes to their efficacy. The waters prepared from the essential oils form agreeable flavouring vehicles.

1. Aromatic Sub-group

Oleum Menthæ Piperitæ (B.P., U.S.P.) ½–3 min. (3–18 cl.). The oil distilled from peppermint, Mentha piperita. Owing to the large percentage of menthol in this oil, it produces an agreeable coolness in the mouth as well as the aromatic pungent taste characteristic of the essential oils as a class. It does not produce a leucocytosis as do the other essential oils (Binz). Its *Aqua* is probably the most popular flavouring vehicle, and the *Spiritus* (B.P.) (10 per cent. of the oil in 90 per cent. alcohol) 5–20 min. (3–12 dl.), one of the most popular and efficient of the carminatives.

Cinnamomi Cortex (B.B., U.S.P.), the dried bark of Cinnamomum zeylandicum, contains an oil and also tannin. Neither the oil, *Oleum Cinnamomi*, ½–3 min. (3–18 cl.), nor cinnamic aldehyde, *Cinnaldehydum*, 1 min., of which it is chiefly composed, are greatly used. The *Aqua* (B.P.) is, however, a useful flavour; and the *Spiritus* (10 per cent. of the oil in 90 per cent. alcohol), 5–20 min. (3–12 dl.), and the *Tinctura* (B.P.), a 20 per cent. percolate of the bark), ½–1 fl. dr. (2–4 ml.) are useful carminatives. The latter is especially used in diarrhœa mixtures. *Pulvis Cinnamomi Composita* (B.P.), 10–60 gr. (6–40 dg.), containing cardamoms and ginger) is a favourite ingredient in intestinal astringent powders.

Caryophyllum (B.P., U.S.P.). Cloves. The dried flower-buds of Eugenia caryophyllata, contains an oil and some tannin. *Oleum Caryophylli*, ½–3 min. (3–18 cl.), contains about 80 per cent. of *Eugenol*, 1 min. Though perhaps not greatly employed as gastric carminatives, these two substances are frequently employed in the preparation of laxative pills; as antiseptics and anæsthetics in toothache and dentistry; and as mild rubefacients in ointments. The *Infusion* (B.P.), ½–1 fl. oz. (15–30 m.), is now rarely used.

Anæthi Fructus (B.P.). Dill. The dried ripe fruit of Peucedanum graviolens. The *Aqua* (B.P.) is a useful carminative for young children, on account of its sweet aromatic taste. The *Oleum* (B.P.) is little prescribed.

Coriandri Fructus (B.P., U.S.P.). Coriander. 5–15 gr. (3–10 dg.). The dried ripe fruit of Coriandrum sativum. Its *Oleum* (B.P.), ½–3 min. (3–18 cl.), has an agreeable taste, and is used as an intestinal carminative.

Cardamomi Semina (B.P., U.S.P.). Cardamoms. The dried ripe seeds of Elettaria Cardamomum. The *Compound Tincture* (B.P.), ½–1 fl. dr. (2–4 ml.), is frequently prescribed as a carminative and flavouring, and, on account of its containing cochineal, as a colouring.

Oleum Lavandulæ (B.P., U.S.P.). ½–3 min. (3–18 cl.). The oil distilled from the flowers of Lavandula vera. The *Spirit* is employed as a flavour, and, owing to its containing red saunders wood, the *Compound Tincture* is used as a colouring ingredient.

Oleum Menthæ Viridis (B.P., U.S.P.), ½–3 min. (3–18 cl.). The oil distilled from spearmint, Mentha Viridis. Its *water* is a useful flavour.

Anisi Fructus (B.P., U.S.P.). Anise. The dried ripe fruits of Pimpinella anisum. The flavour of anise is no longer popular, and the *oil*, *spirit* and *water* are seldom used.

Rosæ Gallicæ Petala (B.P., U.S.P.). The preparations, *confection*, *infusion*, and *syrup* of rose petals are only rarely prescribed. The *oil* is too expensive for use, but its *water* is still employed rather to give odour to lotions and ointments than for mixtures for internal use. The *ointment* is not so frequently employed as a base as formerly.

Carui Fructus (B.P., U.S.P.). Caraway. The dried ripe fruit of Carum Carvi. The *oil* and *water* are no longer popular.

Myristica (Nutmeg). its *oil* and *spirit*; *Fœniculi Fructus*, (Fennel) and its *water*; *Anthemidis Flores* and their *oil* are rarely used.

2. Bitter Aromatic Sub-group

These contain, as well as their aromatic taste, a bitter one, due either to the oil or some other principle. This makes them more useful flavours than the above group, though they are less active carminatives.

Aurantii Cortex Recens (B.P.). Orange peel. Its preparations, especially the *Syrupus Aurantii*, 30–60 min. (2–4 ml.), are useful flavours. *Syrupus aromaticus*, 30–60 min.; *Tinctura Aurantii*, 30–60 min.; *Vinum Aurantii* are less frequently dispensed.

Aurantii Cortex Siccatus (B.P., U.S.P.), its *Infusion* and *Compound Infusion*, Orange Flower Water (*Aqua Aurantii Floris*) and its *Syrup* are now rarely employed.

Limonis Cortex (B.P., U.S.P.) The essential oil, *Oleum Limonis*, possesses a pleasant bitter aromatic flavour. The *Syrup* and *Tincture*, 30–60 min., are both employed, the oil but little.

3. Pungent Sub-group

Capsici Fructus (B.P., U.S.P.). Red Pepper. Contains an essential oil, and also pungent crystalline bodies, which are of greater importance, and to which both the carminative and also the mild rubefacient action which leads to its occasional use in ointments are due. The *Tincture*, 5–15 min. (3–10 dl.), is used in 1–2 min. doses as a carminative and also as a covering for the disagreeable taste of many salts, *e.g.* bromides. The *ointment* is made with a mixed base of spermaceti and olive oil.

Zingiber (B.P., U.S.P.). Ginger. Owes its aroma to an essential oil and its pungency to a resin. Its *Tincture*, ½–1 fl. dr., is a very useful carminative, and the *Syrup* a good covering flavour.

Piper Nigrum. Black Pepper and its *confection* (B.P.); *Armoraciæ Radix*, Horse Radish and its *compound spirit* in my opinion might well be omitted from the Pharmacopœia.

4. Malodorous Sub-group

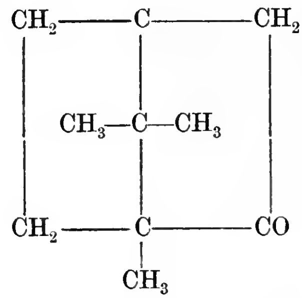
Pharmacopœias include no drugs that seem more clearly the remnants of bygone superstition than the members of this group. It is, perhaps, true that some patients can be influenced suggestively, and like the "poor Indian," still believe that an unpleasant smell and nauseous taste are indicators of a "heap powerful medicine," but surely modern physicians can produce the effect desired by drugs less abhorrent in origin than musk, and less repulsive in odour than assafetida. It is true that Valerian in large doses depresses the central nervous system (Binz), but this can be more effectively produced by other drugs, and its pharmacopœial doses have no determinable effect.

Asafetida. 5–15 gr. The *Pilula Aloes et Asafetidæ*, and the *ammoniated tincture* prepared from *Valerianæ Rhizoma*, are more commonly employed than *Sumbul Radix* and its tincture, *Moschus* (Musk) or Sagapenum.

Stearoptenes: *Camphor, Menthol, Borneol, Thymol*

The action of these crystalline bodies obtained from the essential oils resembles in a general way that of the terpenes. Camphor is much the most employed, and its action is typical of the others.

Camphor (B.P., U.S.P.), 2–5 gr. (12–30 cg.), is a volatile crystalline solid, obtained from the oil of Cinnamomum camphora. Its graphic formula is—



The commercial variety is dextrorotary, but a less active lævorotary form has also been prepared. It is readily soluble in oil or in fats (in milk to the extent of one part in about thirteen), in equal weights of alcohol or one part in 1000 in water.

It has a mildly antiseptic action and is rapidly toxic to many lower forms of life. Its vapours induce in insects depression followed by death. When rubbed into the skin, it manifests a mild rubefacient action and is consequently a common ingredient of liniments.

In the mouth it has a hot, bitter taste, and acts in both stomach and intestines as a carminative. Large doses are apt to produce irritation with nausea and vomiting.

Nervous System.—Some slight stimulation of the central nervous system is produced by small doses, 10–15 gr. per ounce (or 5–10 gr. hypodermically); both higher animals and man seem temporarily brighter and more active after it is given. The respiratory centre is also stimulated. With larger doses 40 gr. or more, the excitement in man is usually much more marked, and is accompanied by some confusion of ideas. Headache is commonly present; inco-ordination of movement, tremors and even convulsions may supervene. Similar convulsions can be obtained in the

higher animals, but do not occur, or are abolished if the cerebellum be destroyed or the spinal medulla cut. They seem to be undoubtedly of cerebral origin.

Circulatory System.—Small doses have little and inconstant effects on the circulatory system when normal (Seligmann, etc.), flushing of the face and neck being the most constant. Toxic doses decrease both the rate, and, to a less extent, the contractility of the heart. There is also a fall in blood pressure (Seligmann, Winterberg, cases of poisoning). The temperature falls slightly.

Excretion.—It is excreted to a very small extent by the lungs and the skin, but chiefly by the kidney. In the urine it is found as a glycuronate of an hydroxyl of camphor, camphorol, and as an amine, camphoral (Fromm and Hildebrandt, Pellacani, etc.).

Its employment apart from its rubefacient and antiseptic actions may be rationally based on the following experimental data, with which clinical experience in the main agrees.

1. A rabbit to which such a hypnotic as chloral, urethane, or paraldehyde has been administered, and in which deep sleep and partial loss of reflexes has been produced, may be wakened and apparently restored to normal activity by a subcutaneous injection of camphorated oil. Even if anæsthesia be profound an increase in respiratory rate and temporary increase in reflex excitability is rarely missed.

2. If a cat's heart when perfused beats weakly or irregularly, and especially if it shows fibrillation, it is often restored by the additions of small amounts of camphor to the perfusion fluid. Seligmann and Gottlieb found this to be a constant effect; Klemperer found it irregular, but agrees that it undoubtedly decreases the ease with which fibrillation may be produced. Winterberg failed to confirm these results. The author has, however, noted cessation of fibrillation under similar conditions.

3. In many cases hearts which are beating more rapidly than normal are slowed. Even in normal men, 10–15 gr. may decrease the rate a few beats, and in some experiments the decrease in rate has been accompanied by an increase in force (Maki, Wiedemann, Pellacani).

4. In certain stages of chloral poisoning in frogs, the heart beats very slowly, but with normal, or almost normal, force. The application of camphor restores the rate approximately to the normal (Bœhme).

These experiments indicate that camphor may be useful in cases of respiratory and cardiac depression due to chloral, chloroform, and other drugs of this group. Clinical experience seems to show that it may possess a similar beneficial action in some fevers. The experiments also indicate that camphor may relieve or prevent acute cardiac fibrillation. A fine suspension suitable for intravenous administration can readily be prepared by agitating an alcoholic solution with normal saline. Its action when given intravenously is much more prompt than when given subcutaneously in solution in oil, and very much more so than when given by the mouth.

The *Water* (B.P.) is used at times as a vehicle for eye-lotions. The *Liniment* (B.P.), camphorated oil, a 20 per cent. solution in olive oil, prepared fresh and sterile, is the best form for hypodermic administration; 10–40 min. may be given. (U.S.P. preparation is made with cottonseed oil.) The *Ammoniated Liniment* (B.P.), containing lavender and ammonia, and the *Liniment of Soap* (U.S.P.) are very commonly employed. The *Spirit* (5–20 min.) is still used when camphor is given by the mouth. The action of the *Compound Tincture* is due to the opium it contains.

Camphoric Acid (U.S.P.), 15 gr. (1 g.), which was supposed to depress the endings of the sweat nerves, has been employed to relieve the night sweats in phthisis. It has no effect upon the sweat nerves, and its sole pharmacological action seems to be a slight stimulation of the respiratory centre (Roth).

Menthol (B.P., U.S.P.), ½–2 gr. (3–12 cg.), is the stearoptene from peppermint oil. It is very slowly absorbed, and very irritant to the stomach and intestines, and hence is not used internally. It penetrates the skin rapidly, especially if rubbed on; and first stimulates the specific endings for the sensation of cold, and then depresses all sensory endings, producing a numbness. Either in the form of a stick or in alcoholic solution it is rubbed on the skin of the sensitive area in neuralgia. Its action is no doubt in part reflex (see *Rubefacients*), in part suggestive. The *menthol plaster* is little used.

Thymol (B.P., U.S.P.), ½–2 gr. (3–12 cg.), is the stearoptene from the oil of Thymus vulgaris and other plants. It is very slightly soluble in water, 1–1500; but has a marked antiseptic action. It is now but rarely used in surgery. Its volatility and antiseptic action lead to its employment in treating ringworm. It is but slowly absorbed from the alimentary canal, and being not very irritant to it, is consequently employed as a vermifuge for Anchylostoma duodenale and Ascaris lumbricoides. Dose: 15–30 gr. (1–2 g.). When absorbed, it is excreted partly in the urine, as an unknown body, which turns green on exposure to the air.

Borneol and *Brom-camphor* differ little from camphor in action, and seem to possess no

action which makes them more advantageous for medicinal use (Lippens). *Apiol*, parsley camphor, is very irritant to the kidneys and the pelvic organs. In Pulsatilla another highly irritant camphor, as well as other irritant bodies, is found.

Drugs acting on the Skin

The intact skin has, as its outer coat, a stratified layer (Stratum corneum and lucidum) of much shrunken and chemically altered cells, which acts both as a physical and chemical barrier to the absorption of drugs. Such absorption as does occur seems to take place largely, if not entirely, through the living cells which line the hair-follicles and the ducts of the skin-glands, unless the drug in question is of such a character as to alter chemically and break up the corneal layer, *e. g.* salicylic acid. Normally, too, the skin and the walls of its capillary recesses (ducts and follicles) are coated with a thin layer of grease, and hence watery solutions do not actually come in contact with it (do not "wet" it); and will not enter the recesses save under considerable pressure. Absorption by a living membrane of any drug can only be expected when two conditions are fulfilled, namely, the drug or its solvent must "wet" the membrane, and further, the drug must be soluble in the membrane or enter into chemical combination with it. If a drug is in solution, its relative solubility in the solvent compared with its solubility in the membrane may also influence its absorption. Vigorous cleansing with soap or fat solvents may remove the fatty layer from the general skin surface, and massage may displace some of the contents of the recesses, but can hardly empty them. Fat solvents, ether, chloroform and alcohol readily penetrate the recesses (capillarity will lead, indeed, to their exerting considerable force in entering) until checked by the contents. Fatty and oily bodies will, of course, "wet" the skin, and may, if fluid enter, or if more solid, be rubbed into the recesses, without great difficulty.

Many volatile drugs, some of those soluble in fat solvents, and some of those soluble in fats, penetrate the skin in a greater or less degree; but few in quantities sufficient to produce general effects. Many, however, exercise local actions. The broken skin, of course, absorbs many drugs with greater readiness than the normal skin can do.

1. *Producing General Effects.*—Prolonged application of strychnine in water or oily solution to the skin of rabbits produces no effect, but if the skin has been first cleansed with ether or chloroform, a slight absorption occurs from a watery solution (Winternitz). Lithium chloride is absorbed from an alcohol-ether solution, but not from an aqueous one by rabbits (Winternitz), nor by man, even after prolonged application (Hüfner). As the spectroscope makes possible the detection of minute quantities of lithium, the inference that ordinary salts are not absorbed may fairly be drawn. Potassium iodide and sodium salicylate, even after prolonged application are not absorbed from a watery solution, nor from ointments (Ritter). In regard to the alkaloids the best evidence is to be drawn from cases of poisoning. Severe or fatal intoxication has occurred due to atropine absorbed from plasters (Smithson, Aldersmith) and by morphine from its tincture (Erben).

Such volatile fluids as aniline, nitrobenzol (Stone), nicotine (Lewin), have also been absorbed by the skin in quantities sufficient to produce poisoning. Mercury and its salt are also absorbed. Mercury is probably acted upon by the fatty acids of the skin and transformed into salts, and the salts of mercury are soluble in fats and also form more or less soluble salts with proteins.

2. *Producing Local Effects.*—Local effects may doubtless be produced on sensory endings by the application of atropine, and possibly by cocaine and other alkaloids, if employed in suitable solvents. Mercury, iodides and iodine, salicylic acid and its esters may also be absorbed in quantities sufficient to affect localised conditions, but such drugs as lead, from its solution and plaster, and zinc can only act upon the surface.

The more important local actions by drugs, applied to the skin, are considered in the following paragraphs, a typical description of the kinds of action being first given, followed by brief notes on the individual drugs employed to produce them—

Rubefacients.—Essential oils and many other volatile drugs penetrate the skin and set up sensory stimulation, the effect of which is a dilation of the vessels, due to a local reflex. It occurs even if the posterior root supplying the area be cut, but not if it be allowed to degenerate, nor if the sensory endings are depressed by anæsthetics or cold (Bayliss, Spiess, Bruce). This dilatation constitutes the first stage of an inflammatory process, and is succeeded by increased exudation of fluid from the vessels (rubor, turgor), and by diapedesis, especially of the leucocytes. Drugs producing these changes are termed "Rubefacients." Bier's epoch-making studies have led us to realise how important these changes are in promoting tissue repair and the relief of pain. The experiments of Wechsberg show this effect in a practical manner. He produced inflammation by injection into both hind- or fore-feet of animals of equal amounts of some irritant; and treated

one foot with a rubefacient application. Cure was more rapid in the part so treated.

Many rubefacients, if allowed to act for a longer time or in greater concentration, produce such an accumulation of fluid that the corneal layer is lifted by it, thus forming a blister. This action is termed vesication and the drugs are called Vesicants. Within the blister cytolytic changes occur rapidly, and some invasion and destruction of leucocytes takes place. It is probable that when this occurs, the vessel walls have been damaged by the irritant. Some of these drugs cause a marked local leucocytosis and rapid cell degeneration, producing numerous "pustules." They are consequently termed "Pustulants."

If the stimulation be more intense or more prolonged than that necessary to produce mild local reddening, more distant reflexes occur. The studies of Head have led us to understand how close the central connection is between each of the internal organs and the skin area whose sensory supply comes from the same segment of the central nervous axis. Sensory irritation of any viscus is referred to a certain skin area, and, indeed, this area often shows a marked hyperæsthesia if the viscus be the site of inflammation. The reflex effect produced by marked stimulation of any skin area seems to be an increased blood supply to the associated viscus, the reverse of what was formerly implied when rubefacients were used for their so-called "derivative" effect.

Skin stimulation, if intense, produces readily observed general reflex effects, increase in respiration, heart-rate and blood pressure, which, usually, are succeeded by decrease in pressure and a slower pulse. With less marked stimulation, these effects are slighter, but some increase in respiratory rate and increase in general metabolism are shown by the experiments of Röhrig and Zuntz, Paalzow, Heidenhain.

The *Essential Oils* all produce rubefaction, but turpentine and mustard are those most commonly employed.

Turpentine has great penetrating power, and acts fairly rapidly, but is not very irritant, and does not produce blisters quickly. These, if formed, however, heal but slowly and are painful. It is chiefly employed in the form of liniments or the "turpentine stupe." This is best prepared by wringing flannel out of hot water, sprinkling with turpentine, and applying while hot. Rubefaction is produced in ten to twenty minutes.

Mustard (U.S.P.). Sinapis. The dried ripe seeds of Brassica niger and alba. Both Sinapis Albæ and Sinapis Nigræ Semina are official. The white mustard contains a glucoside, sinalbin, which is in itself inactive, but which is hydrolysed by the action of an enzyme, myrosin, contained in the seeds, in the presence of water to produce acrinyl-isothiocyanate (a volatile oil), dextrose and a complex body, sinapin acid-sulphate.

$$C_{30}H_{42}N_2S_2O_{15} + H_2O = C_7H_7ONCS + C_6H_{12}O_6 + C_{16}H_{24}NO_5HSO_4$$

Black mustard seeds, containing the same ferment which similarly hydrolyses its glucoside, sinapin, produces allyl-isothiocyanate, C_3H_5NCS, dextrose and potassium acid-sulphate. *Oleum Sinapis Volatile* (B.P., U.S.P.) should contain 92 per cent. of allylisothiocyanate. Both oils have a similar intensely irritative action, producing blistering in a minute or two. They rapidly destroy any tissue with which they are brought into contact. Their fumes are intensely irritating. Large doses taken internally cause an intense gastro-enteritis. Mustard is frequently employed as an emetic, as it acts quickly: a tablespoonful in water is given. When used as an emetic, it is best to stir the powder rapidly in cold water and have it taken at once, as this tends to avoid some of the burning in the mouth and throat. For its rubefacient action mustard is commonly used either as plaster or a poultice. The latter is prepared either from the powdered seeds alone, or if a weaker and more slowly acting poultice be required, from flour into which mustard has been stirred. The powder is mixed with water to a thick paste and spread on cheese-cloth. A burning pain and rubefaction is produced in fifteen to thirty minutes. When the poultice is removed, the skin should be wiped to remove the oil. The *Liniment* is not very frequently employed.

Cantharis (U.S.P.). Spanish Fly. The dried beetle, Cantharis vesicatoria, contains a crystalline substance, *Cantharidinum* (B.P.), which is a lactone of cantharidic acid. It is very slightly soluble in water, but its salts are soluble. It is sparingly soluble in alcohol, and only slightly soluble in fats. Rubefaction is produced very slowly, not for three to four hours, and vesication, for which it is chiefly used, not for eight to ten. The *plaster* should be removed while the vesicles are still small and discreet, since as they contain some cantharidin, vesication will continue, and a large bleb arise.

Internally, cantharidin is intensely irritant, readily producing severe vomiting and purging with bloody stools, and often collapse with low blood pressure and congested abdominal organs. It seems to be excreted by the intestinal canal, since subcutaneous injections lead to intestinal irritation. It is excreted by the kidney, to which it is intensely irritant, producing a rapid congestion and tubular degeneration, to which glomerular changes, if produced, are but secondary (Susuki, Mackenzie). In alkaline

urine it seems to be less irritant. Cases of poisoning now most frequently occur owing to its application to the broken skin, by which it is rapidly absorbed. Albuminuria and often anuria are produced. The use of cantharidin internally seems hardly justifiable, nor does its employment by hypodermic administration seem to give better results than can be obtained by other means. The official *Plasters* are being replaced by those prepared from purified cantharidin and a rubber base. The *Ointment* will hardly produce blistering. The *Tincture*, alone, is used internally, and is also employed in hair lotions. The *Collodions* are sometimes useful when a plaster could with difficulty be applied.

Iodine in the form of the tincture is one of the most useful rubefacients, as it acts quickly and deeply, its volatility and chemical activity make frequent application necessary if a continued action is desired, but increases the ease with which the amount of rubefaction can be controlled.

Capsicum ointment has a mild rubefacient action, and even prolonged application rarely leads to blistering.

Chloroform and *Ammonia* have a decided rubefacient action, especially if their vapours be confined, or if they are well rubbed into the skin. They are very common and useful ingredients in liniments. Their action is, however, very evanescent.

Croton oil is, perhaps, the best pustulant, but is very rarely employed.

Oil of Wintergreen, Methyl Salicylas (Ol. Gaultheriæ), penetrates rapidly and is employed in liniments and ointments for rheumatism.

Oil of Rosemary gives a very pleasant odour to ointments and is still at times employed for that purpose; it is too irritant to be given internally and its use might well be discontinued. The same may be said of Mezereon, whose irritant principle produces rubefaction but slowly. The preparations of arnica, especially its tincture, are much esteemed in household medicine. Their rubefacient action, however, is slight. The same may be said of preparations of Hamamelidis Cortex, Witch Hazel, probably amongst the most inefficient remedies exploited by the pharmaceutical houses. The alcohol, with which they are prepared, seems to the author to produce equally good effects.

Thiosinamine, allyl-thio-carbamide, $C_3H_5NH.CS.NH_2$, is a body prepared by heating oil of mustard, ammonia, and alcohol. It was first employed as a hypodermic injection to promote the absorption of scar tissue by Hebra; and has been used in glycerin solution and in ointment to promote the healing of lupus. Clinical reports are by no means unanimous, and it does not seem to be gaining in favour. In digestion experiments, it increases the rate of transformation of tendon into gelatine (Starkenstein).

Ointment Bases

The absorbability of ointment bases and their usefulness in promoting absorption of drugs have been frequently investigated, with varying methods and correspondingly varied results. It seems clear, however, that the paraffins, even when liquid, are not absorbed (Wild); but they may penetrate into the skin recesses (Unna, Sutton), while lard and hydrous wool fat (Lanolin) are also absorbed to a considerable extent, if well rubbed on (Wild, Sutton, Gardiner). Olive oil is also absorbed, and a mixture of olive and lanolin, or of the latter and cedar oil even better. Clinical experience confirms the experiments of Wild that paraffin ointment is not of great value for any purpose; and cetaceum is now but seldom employed. The experiments of Sauerland throw a new and important light upon the whole question of the necessity of employing an absorbable base to obtain the absorption of a drug. As pointed out above, all that is needed is that the base bring the drug into contact with the absorbing cells. The drug absorption will then depend on the relative solubility in the cell on the one hand and in the base on the other. In his experiments Sauerland found that less iodine was absorbed from a lard than from a vaseline ointment; and still less from one made with lanolin. As lard has a higher iodine value than lanolin, the result cannot depend on a chemical retention of the iodine by the unsaturated fatty acids of the base. Vaseline formed the best base to promote the absorption of methyl-salicylate (Oil of Wintergreen), but not so good for saligenin. It may well be that these results are due to the fact that the more soluble the drug is in the base, the less of it will be absorbed in a given time by the skin; though it must be slightly soluble in the base, in order that it may be brought into contact with the absorbing cells.

Antiseptics and Stimulants

An antiseptic treatment of the skin is made difficult by the roughness of the corneal layer and by its numerous recesses. In the depths of the hair-follicles and gland ducts bacteria readily find a lodging and are protected by its contents from the ordinary antiseptic applied to the surface. Even insects find in the recesses an ample and safe lodging. Careful bacteriological studies have, indeed, clearly shown that absolute sterilisation is impossible (Paul and Sarwey), unless substances are employed in such con-

centration as to cause serious damage to the skin itself. The physico-chemical reasons which explain why sterilisation cannot be obtained have been abundantly set forth in the introductory paragraph of this chapter.

Dermatologists in treating disease of the skin encounter the further difficulty that the skin, when inflamed, and especially when denuded of its corneal layer, absorbs all drugs much more readily than when intact, and in consequence they are forced to employ relatively weak and slightly toxic antiseptics, or to employ the stronger ones in very low concentrations.

The slight irritation and rubefaction that accompanies the local absorption of many of the antiseptics tends to promote fresh growth of the epidermis, and in consequence benefit is derived from the use of some drugs whose antiseptic actions are slight. Further, some of the antiseptic drugs enter into chemical combination with the cells even of the corneal layer, causing in them changes which loosen them from the underlying layers. This so-called *keratolytic* action is often of great value as it permits of a deeper action than would otherwise occur. This action is especially well shown by some of the phenol group and by the alkalies. Alkaline soaps, though irritant, form in consequence much more efficient cleansing and disinfecting solutions for the skin than those which are neutral in reaction.

The tincture of iodine seems to be the most useful antiseptic for the preparation of the skin for surgical procedures, as it penetrates deeply and rapidly, and produces a slightly astringent action, thus decreasing the secretion of glands and preventing the exit of the bacteria from the skin crypts. Alcohol in about 90 per cent. solution is probably the antiseptic, which ranks next in value (Reinicke), though mercuric chloride, or iodide, are also very effective. Neither of these produces the irritation which makes the frequent employment of phenol and its congeners impossible for many people.

When the skin is inflamed, less toxic and weaker antiseptics must be employed, or the stronger antiseptics in very low concentrations, and then the slight irritant action that these remedies all possess seems to equal in importance their antiseptic action as it leads to more rapid growth of normal epidermis. Many drugs, especially resins and gum-resins, were introduced for this purpose, but are used less and less as dermatologists realise the advantage of preparations whose exact composition is known, and in which any active ingredient can readily be omitted or altered in strength.

Resina (B.P., U.S.P.) (resin) consists chiefly of abietic acid, but contains small amounts of various aromatic bodies. It has a very weak stimulant action, and was chiefly used as a basis to give adhesiveness to plasters and at times to ointments. Owing to the introduction of gutta-percha it is now seldom employed for such plasters as are made commercially, and is also less used when extemporaneous plasters are ordered.

Pix Liquida (B.P., U.S.P.) (tar) and *Pix Burgundica* (Burgundy pitch) both contain resins and other aromatic bodies. They also contain small amounts of various phenols, and have in consequence a slight keratolytic action. Their other constituents, however, promote epidermal growth. *Pix Carbonis Præparata* (B.P.) (prepared coal-tar) acts in a similar way but its keratolytic action is somewhat greater. They are all employed chiefly in squamous inflammations, but not so commonly as formerly. The action of *Oil of Cade* (B.P., U.S.P.) is more stimulant and less keratolytic.

Balsam of Peru and more rarely that of Tolu, are employed as mild and slightly irritant poisons in the case of insect infections, *e. g.* scabies. *Ammoniacum, Galbanum* and *Myrrh* are also occasionally dispensed by dermatologists, but the repute in which they were held is declining.

Thus Americanum (Frankincense) and *Terebinthina Canadensis* (B.P., U.S.P.) are occasionally employed to give adhesiveness to preparations that are to be applied to the skin.

Sulphur, as such, has no action, but is gradually transformed by the alkalies and acids of the skin secretions into salts of the sulphides and polysulphides. This change is more rapidly produced when it is prescribed with alkalies. These sulphides possess definite but mild keratolytic actions and are also stimulant and antiseptic. They are useful in scabies but prove most valuable in psoriasis.

Resorcin (B.P., U.S.P.) and *Pyrogallol* (U.S.P.) are also mild keratolytic agents, but both have marked antiseptic actions which make them very valuable to dermatologists.

Ichthyol, a brownish, syrupy substance which is distilled from a bituminous shale found at Seefeld in the Tyrol, possesses many advantages in actual practice over the antiseptic stimulants whose chemical composition is more accurately known. It is much less toxic, doses of 15 gr. per diem may be given internally, and it may hence be used when the skin is broken with greater freedom than any of the phenols.

Chrysarobin (B.P., U.S.P.), a crystalline powder prepared from Andira araroba, is very irritant and is absorbed even by the unbroken skin in small quantities. If greater amounts are absorbed its excretion as chrysophanic acid leads to marked inflammation of the kidneys.

Salicylic Acid (B.P., U.S.P.), though antiseptic, is chiefly applied to the skin on account of its very marked keratolytic action. A 10 per cent.

solution in an ointment base or collodion rapidly softens and loosens the epidermal layer, and it is in consequence of great value in promoting the removal of corns.

Scarlet Red, on the other hand, is chiefly employed to promote the growth of epithelial tissue. Fischer found that by injecting its solution into the skin he could produce overgrowths resembling epitheliomata. Schmieden pointed out its usefulness as a stimulant to the epidermis, and employed it in the form of an ointment to promote the healing of chronic ulcers and burns. The active principle was found to be amidoazotoluol, and this has been extensively employed and apparently with great success by Michælis and others. It is absorbed by the broken skin, and if applied over too large an area may cause poisoning.

Giddiness, headache, vomiting, pains in the abdomen, cyanosis, albuminuria and increased pulse rate were the symptoms observed (Gurbski). An acetyl derivative, known as azodermin, has been tested in both animal experiments and in practice, and is reported as being less toxic but equally efficacious in promoting epithelial growth (Kurchmann).

To produce similar stimulant effects on the epidermis, Macallister has called attention to the common Comfrey, Symphytum officinale, attributing its action, in part at all events, to the large percentage of allantoin it contains. Its beneficial action in promoting the healing of wounds has been confirmed by other observers.

Glycerin may, perhaps, also be classed among those drugs that tend to promote the healing of wounds. Owing to its marked hygroscopic properties it extracts water from the skin, and, especially if the skin be broken, causes a tingling and some redness. This action in itself tends to promote healing, but in addition it tends to keep the skin moist by retaining water, and hence prevents that marked drying which so frequently leads to chapping when the skin is exposed to dry and cold air. To prevent chapping it is, perhaps, best diluted with water or incorporated in an ointment.

Drugs with Secondary Actions on the Skin

Very many drugs which have no action upon the skin when applied to it, and many others whose local action upon it are almost negligible, manifest, especially in certain persons, very marked secondary or remote skin effects. The facts necessary for a scientific classification are in many cases wanting. Even in those cases where we assume that the action is due to the presence of the drug in question in the skin, very little evidence of this has been forthcoming. In large part this is explained by the fact that we cannot reproduce these lesions in laboratory animals; and even in man they occur only in certain exceptional individuals. Nor can we, in many cases, explain the idiosyncrasy that such individuals manifest. These secondary remote actions can, however, be roughly classified from a pharmacological view point in the following way—

1. The intense localised erythema with subsequent desquamation, seen so typically in scarlet fever, is paralleled very closely by the secondary action of atropine. This drug produces, owing to its action on the central nervous system, a marked dilatation of the vessels of the skin, especially over what may be termed the "blush area," the skin of the face, neck and upper part of the chest. We have no definite knowledge whether this is due to central depression of the vaso-constrictor centre, or stimulation of certain vaso-dilators. The latter appears, however, more probable. The effect is doubtless increased in the case of atropine by the depression of the secretory endings in the sweat glands, so that the cooling of the skin, due to evaporation, is less than normal. The similar lack of secretion, doubtless, contributes to the intensity of the erythema in scarlet fever. A centrally produced vaso-dilatation may well play a part in the erythema seen in chronic strychnine poisoning, and in that occurring subsequent to the administration of analgen, antipyrin, colchicum, aconite, conium, cocaine, solanin and morphine.

2. In the case of other poisons, the erythema is doubtless due to a peripheral effect on the vaso-constrictor endings in the vessels or on the musculature of their walls, though possibly due to a central action, as in the first group. Chloral, we know, depresses the vessels peripherally. In this group may be included: chloral, veronal, sulphonal, picric acid, copaiba, quinine, nitroglycerin, chloroform and arsenic.

3. The scientific data necessary for the explanation of a further group, which may be described as those drugs that acting on the skin alter the relative proportion of its salt bases, is rapidly accumulating. The symptoms of oxalic acid poisoning are referable, in the main at all events, to disturbances in the calcium content of the body organs (Chiari and Fröhlich, Chiari and Januschke, Luithlen). The eczema of dogs is always of a dry type; but if an animal be given a sublethal dose of oxalic acid, eczema of a moist character develops. Deficiency in calcium leads, apparently, to a greater permeability of the vessel wall (Chiari and Januschke, and also changes the irritability of its nerve-endings for chemical stimuli (Chiari and Fröhlich). Mercury calomel, or corrosive sublimate, alters the calcium content of the intestinal mucosa (Chiari), and may well alter that of the skin. The same action may be exerted by lead and bismuth. To this the erythemata

of oxalic acid, corrosive sublimate, chronic lead and of bismuth poisoning may be ascribed.

4. Certain other drugs, whose action at present cannot be so readily explained, also seem to increase greatly the permeability of the vessel wall, and lead either to a more or less marked general skin eczema, to œdema of the eyelids alone, or to urticaria. Such are copaiba, cubebs, santal, eucalyptus, ipecacuanha, santonin and antitoxic sera. The eating of crabs, eggs, veal, and occasionally other foods affect certain persons in a similar fashion.

5. The skin possesses a great capacity for storing up chlorides, in which it is normally very rich (Padtberg). Here, as elsewhere, the replacement of chlorides by other anions, especially of the halogen group, will readily occur. If bromides or iodides be administered in full therapeutic doses, they may readily be found in increased amounts in the skin. In how far their presence primarily influences the vascular condition we do not know; but as they will replace in part the chlorides of the normal secretions, they may be broken up by any fatty acid produced by decomposition of the fat secreted, and the irritant halogen acids, or free halogens produced may act as rubefacients. The erythemata which sometimes occur when iodides, potassium chlorate and iodoform are administered may, perhaps, be explained in the light of the above facts. These also make comprehensible the morbilliform rashes that occur when bromides and iodides, benzoic acid, salicylic acid and acetyl-salicylic acid are being administered.

6. We have reason to believe that many drugs may be found in the secretions of the sweat and sebaceous glands. The fundamental cause of the secretion of iodides and bromides is to be found, as shown above, in the replacement, in part, of the chlorides normally present. The excretion of many other bodies is doubtless due to their ready diffusibility rather than to any secretory action. This is probably the explanation of the erythemata, often morbilliform in character, due to alcohol, urotropin, nitroglycerine, benzol, turpentine, camphor, copaiba cubebs, santal and some other essential oils.

7. Certain drugs produce marked effects on skin glands. Atropin, carbon monoxide, boracic acid, arsenic and lead decrease these secretions. Pilocarpine and physostigmine increase their activity, and the former is said, at times, to lead to an inflammation.

8. Skin necroses and degeneration, probably due to muscular spasm of the vessels, or secondary to vascular disease, are seen in chronic poisoning by ergot, arsenic, carbon monoxide and phosphorus.

9. Skin thickenings, keratosis, are sometimes observed after the continued use of arsenic.

10. Pigmentation of the skin is often caused by such drugs as produce methæmoglobin and hæmatin, *e. g.* aniline, nitrobenzol, phenacetin. Bromides, arsenic, and some other drugs also occasionally cause a brownish pigmentation, which may also be due to a broken-down blood pigment. Silver, if given internally, is set free from its protein or other combinations, by the action of light; and is deposited in the skin, as greyish specks, argyria.

V. E. H.

FOOD DRUGS

Oleum Morrhuæ (B.P., U.S.P.) (Cod-liver Oil)

Cod-liver oil is extracted from the fresh liver of the cod, Gadus Morrhua, by the application of low pressure steam at a temperature not exceeding 85° C., after which it is cooled to −5° C., and the frozen mass submitted to pressure in canvas bags, the purified oil being forced through the canvas, and a whitish tallow-like mass of so-called "stearine" and liver debris, being left in the bags.

Spec. gravity 0·92–0·93.
Refractive index at 40° C., 1·4704–1·4745.
Iodine value 155–173.
Saponification value 179–192.
Dose : 1–4 fl. dr. (4–16 ml.).

Constituents.

	Palmitic acid 4 per cent.
Oleic acid series $C_nH_{2n-2}O_2$	Jecoleic acid ($C_{19}H_{36}O_2$) 20 per cent.
	Gadoleic acid ($C_{20}H_{38}O_2$).
	Erucic acid ($C_{22}H_{42}O_2$).
$C_nH_{2n}O_2$ series	Therapic acid ($C_{17}H_{26}O_2$) 20 per cent.
	Cholesterol 0·5 to 1·3 per cent.

The fatty acids are present as glycerides, although there is always a small quantity of free fatty acid. Very small quantities of iodine and phosphorus are present.

Older forms of cod-liver oil, which, in preparation, were heated to a higher temperature, or were allowed to undergo oxidation changes, or were not prepared from the livers of cod freshly killed, were deeply coloured, very malodorous and distasteful. They contained oxy-acids, large percentage of free fatty acid, and organic bases of the ptomaine type.

For reasons given below, the less coloured and more tasteless the oil, the more efficacious it is in treatment.

Nature of Action.—The fundamental difference between the pharmacological action of cod-liver oil and most other drugs, is that, whereas the latter alter the dynamic condition of living tissues by causing chemical and physical changes in the cells, without supplying any but a negligible quantity of energy themselves, cod-liver oil is taken up by the cells and supplies its large

amount of energy for the general economy of the tissues. Undoubtedly the beneficial effects of cod-liver oil are, for the most part, to be explained by its exceptional value as a foodstuff and as a source of energy. Being a fat each gram can supply to the body 9·2 calories, whereas a gram of carbohydrate, such as starch or glucose, can only supply 4·4 calories, and a gram of protein 4 calories. As a foodstuff, however, fats present obvious disadvantages, particularly to those unaccustomed to eating them, and these disadvantages, although very much smaller in the case of cod-liver than with ordinary subcutaneous and other depôt fat, are by no means negligible. In the first place, the well-nourished person in a temperate climate dislikes much fat, and since there is no truer indication of mental attitude than that reflected in the alimentary canal, it is not surprising that fats are known not only to inhibit the movement of the stomach, but also to diminish the secretion of the gastric juice, and therefore of the pancreatic and other digestive juices of the intestine. Not only do ordinary fats derange the digestive system, but the power of the intestine to absorb them is limited, so that with very large quantities of fat in the food, much of its energy is wasted because it is not absorbed. Now with cod-liver oil these deleterious effects are very much less than with other fats, so that in most cases it is possible to derive all the advantages without experiencing the drawbacks associated with ordinary fats. Cod-liver oil, even when taken in large quantities, is nearly all absorbed, and not only so, but Williams has adduced evidence to show that it even aids the absorption of other fats in the food, so that, when cod-liver oil is added to a standard diet, less fat is excreted. The fact that it is more readily absorbed than other fats implies that its inhibitory action on the other digestive actions is much smaller. The ready absorption of cod-liver oil by the intestine is, no doubt, largely explained by two factors. In the first place all its constituents have a low melting point, and secondly it contains small quantities of free fatty acid, which ensures immediate emulsification, when it meets the alkaline juice of the intestine. It is well known that thorough emulsification is the preliminary stage to fat absorption, and this emulsification is brought about when free fatty acid, as is present in cod-liver oil, meets the sodium carbonate of the pancreatic juice and bile.

The digestive advantages of cod-liver oil over other fats are not the only ones, for the metabolic advantages have, in consequence of recent physiological research, been shown to be equally important. The work of Leathes has made it clear that before the subcutaneous fat found in animals is used by the different organs of the body, it is mobilised in the liver and subjected to various changes, one of which, namely, the conversion of the saturated fatty acids such as palmitic and stearic and to the unsaturated fatty acids of the oleic, linoleic, linolenic, etc., series, is understood. Now this preliminary stage of desaturation has already been undergone in the case of cod-liver oil, so that, in taking this kind of fat, we have a form which can be immediately burnt in the body and made use of as a source of energy. In the above account of the chemical composition of cod-liver oil it is seen that it is almost entirely made up of unsaturated fatty acids, and its iodine value—the number of grams of iodine that can combine with 100 gm. of the oil—which is a measure of the amount of unsaturated acids, is 160 compared with 80, the iodine value of subcutaneous fat, and 50 that of butter. Incidentally, it may be mentioned that too much reliance must not be placed on the iodine value of a fat from the standpoint of digestion, for there can be little doubt that butter fats, with the lowest iodine value, are as easily digested as any other. This may be correlated with the large amount of volatile fatty acids of low melting point which butter fats contain. How far the desaturation of fatty acids in the liver goes on is not known, but Leathes and Meyer Wedell have shown that, even when cod-liver oil is given to cats, the liver fats, a few hours later, are more desaturated, and therefore have a higher iodine value than the original oil.

Further evidence of the ease with which cod-liver oil is assimilated by the body is afforded by the well-recognised fact that adiposity, following the ingestion of cod-liver oil, quickly disappears, when the individual ceases taking the oil, and since Lebedeff's experiments of feeding dogs with linseed oil, it is known that the nature of stored subcutaneous fat is similar to the fat of the food.

Apart from any other less understood property which cod-liver oil may possess, its important properties as an easily assimilable foodstuff of high energy value would explain its efficacy in the treatment of conditions of malnutrition and chronic wasting like richets and tuberculosis, for there can be no doubt that the resisting power of any tissue to toxic influences depends on the amount of nutrition it has at its command. Much evidence could be brought forward in support of this fact, but it will suffice to mention the way in which the body reacts when in a condition of toxæmia. The whole general metabolism is raised, the glycogen is burnt up in the liver, and large quantities of depôt fat are transported to the liver to be so desaturated that the body tissues can make use of it as a source of energy. What is indicated in such cases, therefore, is that we should

aid the body in its campaign of resistance by supplying some suitable source of energy as cod-liver oil.

Other properties have been attributed from time to time to cod-liver oil, to explain its value in disease, and particularly in tuberculous affections. For instance, importance has been attached to the small quantities of iodine and phosphorus it contains. Again, some people still think that the older forms of cod-liver oil, which were deeply coloured, very distasteful, and malodorous, were more effective than the modern, nearly colourless and less distasteful forms. Modern samples of cod-liver oil are obtained from the liver in an atmosphere of CO_2, in order to prevent the oxidation of the unsaturated fatty acids to oxy-acids. There can be no doubt that such cod-liver oil has a higher therapeutic value, and the more colourless and less distasteful it is, the greater the amount of unsaturated fatty acids it contains, and therefore the more easily it is metabolised.

In consequence of the hæmolytic properties of unsaturated fatty acids, Williams and Forsyth sought for, and obtained, evidence that some part of the action of cod-liver oil in tuberculosis might be explained by the disintegrating action of unsaturated fatty acids, such as cod-liver oil contains, on the wavy envelope of the tubercle bacillus. One cannot pronounce any opinion on this suggestion, but it may be well to mention that White, Cammon and Hollander have recently stated that rabbits injected with 1 mg. of bovine tubercle bacilli developed more severe lung lesions if treated by the injection of olive oil and cod-liver oil than if untreated.

To sum up, the therapeutic value of cod-liver oil is to a great extent, if not entirely, to be attributed to the fact that it is an easily assimilable foodstuff of high energy value, in consequence of which it is capable of converting a negative nitrogen balance of a wasting patient into a positive one, and further, that in being easily metabolised, it increases the defensive mechanism of the body to infective agencies.

Therapeutics.—From the foregoing account of the physiological action of cod-liver oil, it is clear that the indications for treatment with this substance include all conditions of malnutrition, and it is given with beneficial results in such diseases as rickets and tertiary syphilis, in wasting conditions due to starvation, in chronic illness, after acute infections and in too rapid growth. In all conditions of tuberculosis cod-liver oil is given and patients often improve under its influence. In all these cases not only is the wasting diminished or even changed to a retention of foodstuffs, but the resisting power to the infection is increased so that the general nutrition is improved and the period of convalescence shortened. In bronchitis, and particularly in the chronic form of this disease, cod-liver oil is often beneficial, and it is said to aid the expectoration in addition to improving the general condition. In conditions accompanied by a generally low tone of the body, such, for instance, as neuralgia, sciatica with anæmia and wasting, general despondency and other nervous derangements, cod-liver oil is useful.

Cod-liver oil may frequently be of great benefit in cases of diabetes, particularly when the patient is rapidly losing weight. In such cases a good plan is to estimate the energy value of the sugar excreted and to replace this by an equivalent quantity of oil by the mouth. Large quantities are often well taken by diabetics, especially if gradually increasing doses are given. If the excretion of acetone bodies is increased by this treatment, cod-liver oil is contra-indicated, but this does not usually happen, and the patient's general condition may be considerably improved, the weight increasing rapidly, and the voracious appetite becoming normal.

It will be evident from the account given above of the action of fats on the digestive system, that cod-liver oil must be administered with care. In digestive disorders of the stomach and in cases of diarrhœa cod-liver oil may increase the symptoms. When the patient has an atonic condition of the stomach, as in dilatation, and, generally, when the stomach movements are abnormally slow, cod-liver oil may make the condition worse with the subsequent production of eructations and vomiting. Its unpleasant taste frequently has to be overcome before patients will take it, although many of the best forms, owing to careful manufacture, have but little taste. To this end it may be taken in ether, 10 min. to 2 dr. of cod-liver oil, or with peppermint water. It may also be placed in gelatine capsules. The best way, however, to administer cod-liver oil is in the form of an emulsion, with or without the addition of maltine. It is usual to give it from half-an-hour to an hour after a meal, *i. e.* after the processes of gastric digestion are well started and food has begun to enter the duodenum. It is sometimes advisable to begin with small doses of ½ to 1 dr. and gradually to increase the dose to the desired amount.

The preparations marked with an asterisk are probably the most useful methods of giving cod-liver oil.

Emulsum Olei Morrhuæ (U.S.P.). 2 fl. dr. (8 ml.).

Emulsum Olei Morrhuae cum Hypophosphitibus (U.S.P.). 50 per cent. Cod-liver Oil with Hypophosphites of Sodium, Potassium and Calcium. 2 fl. dr. (8 ml.).

*Emulsio Olei Morrhuæ (B.P.C.). 2–8 fl. dr. (8–30 ml.).

Emulsio Olei Morrhuæ Composita (B.P.C.). Contains no Sugar. 2–8 fl. dr. (8–30 ml.).

*Emulsio Olei Morrhuæ cum Ferro (B.P.C.). 4 gr. of Iron and Ammonium Citrate in each fl. oz. 2–8 fl. dr. (8–30 ml.).

Emulsio Olei Morrhuæ cum Glycerophosphatibus (B.P.C.). 50 per cent. Cod-liver Oil with Glycerophosphates of Calcium, Iron, Magnesium, Sodium and Potassium. 2–8 fl. dr. (8–30 ml.).

Emulsio Olei Morrhuæ cum Hypophosphitibus (B.P.C.). 50 per cent. Cod-liver Oil with Hypophosphites of Sodium and Calcium. 2–8 fl. dr. (8–30 ml.).

*Extractum Malti cum Oleo Morrhuæ (B.P.C.). 15 per cent. Cod-liver Oil with Malt Extract. 1–4 fl. dr. (4–15 ml.).

Emulsion of cod-liver oil is occasionally given with glycerophosphates or hypophosphites. Since glycerophosphates are attacked in the alimentary canal and the phosphoric acid absorbed as a simple salt, there does not appear to be much advantage in using them in preference to the hypophosphites.

Meat Extracts

Preparation.—Many meat extracts are on the market, but, owing to the method of their manufacture, they have certain disadvantages; for, when being evaporated down to a small bulk, their constituents may be chemically changed and not only lose their physiological value but become toxic. For instance, creatin is converted to a basic substance, creatinin, which, on ingestion, instead of being retained by the body, is rapidly excreted. Carnosin may also be hydrolysed to β-alanin and histidin.

Extracts of yeast are also on the market and are very similar to meat extracts. They contain, however, no creatin. They are much cheaper than the proprietary meat extracts, and are probably as efficacious.

An effective way of making a meat extract is as follows—

To 1 lb. of finely minced beef, add 1 pint of cold water; thoroughly mix and set aside for ten minutes. Place the mixture in a pot surrounded by water in a saucepan and gradually raise the temperature of the water to boiling point. Decant the liquid from the coagulated protein. The fat may be skimmed off the surface if the extract is allowed to cool. By this method chemical changes in the extractives are negligible.

Composition.—A typical analysis of a meat extract gives the following composition—

Moisture, 17·12–21·5 per cent.
Mineral Salts, 18·35–26·3 per cent.
Organic matter, 55·34–62·43 per cent.
Total Nitrogen, 9·48–11·62 per cent.
Proteose, 8·52–14·26 per cent.
Peptone, 3·34–5·6 per cent.
Total Protein, 14·12–19·34 per cent.
Creatin and Creatinin, 9–12·5 per cent.
Insoluble matter, 0·25–0·88 per cent.
Sodium Chloride, 2·68–5·69 per cent.
Phosphoric Acid, 3·06–6·7 per cent.

Non-Nitrogenous Extractives.	*Nitrogenous Extractives.*
Glycogen	Creatin
Dextrin	Creatinin
Sugars	Xanthin
Lactic Acid	Hypoxanthin
Inosite $(C_6H_6)OH_6$	Carnitine
Fat	Carnosine
	Novaine
	Ignotine
	Phosphocarnic Acid
	Inosinic Acid.

Mode of Action.—Although the part played by extractives in the animal economy is not yet understood, recent research has served, in the first place, to emphasise their necessity as an article of diet, and, secondly, has indicated the direction in which they exert their activity. That they exert a profoundly beneficial effect on the alimentary canal is well recognised. For instance, by their action on taste and smell they may be directly responsible for large secretions of salivary and gastric juices. This action is purely of a reflex nature, and so far as the stomach is concerned is performed through the vagus nerve. But more than this, Edkins has shown that meat extracts are the best liberators of gastrin from the pyloric and duodenal mucous membrane, and that gastrin is carried in the blood-stream to stimulate a further flow of gastric juice from the fundus glands of the stomach. Thus meat extracts may be responsible for the immediate nervous secretion, and, in addition, for the more prolonged chemical secretion of gastric juice in the stomach. Since the secretions of pancreatic juice, bile and succus entericus depend upon the hydrochloric acid of the gastric juice, it is clear what a profound influence on digestion meat extracts may have. Many years ago Rubner showed that the addition of meat extracts to the diet brought about a more complete absorption of foodstuffs, so that the stools had less chemical energy when extractives were eaten with a constant diet. It remained for Pawlow and his school to add the explanation of this fact by demonstrating the stimulating effect of extractives on the digestive juices. But besides this action on the alimentary canal, extractives have a marked influence on the

general metabolism. Hopkins has shown that, if young growing rats are placed on a synthetic diet of pure protein (caseinogen), fat carbohydrates and salts, their normal rate of growth is diminished and they die on the sixteenth day; and their death is not due to lack of nourishment, for the caloric value of food assimilated is in excess of their requirements. The addition of small quantities of extractives from meat or milk allows them to live healthily. Similar work has been done by Stepp. These results are most important and clearly indicate that extractives play an important part in bioplasm synthesis incidental to growth as well as in the maintenance of life of the animal. Other work emphasising their importance is seen in the curative effects of a group of extractives known as "vitamine" which are curative of beri-beri, a disease affecting particularly nervous structures which develop as the result of a polished rice diet. The production of scurvy, also, seems to depend on the absence from the diet of some essential extractive, and the condition generally improves on the addition of fresh meat extract.

One other fact which points to the importance of meat extractives in the diet is the retention of a large part of their nitrogenous constituents by the body, even when there is abundant protein eaten. This fact was shown by Rubner and others, and has recently been developed by Folin and by Thompson. For instance, all the creatin of a diet up to 2·5 gm. per diem is retained absolutely by the body and is not excreted as urea, creatinin, or any other known substance. It is obviously a desirable substance which the body keeps for some purpose not known.

Another fact which, in correlation with the retention of nitrogen of meat extracts, has recently become of public interest is the increase in weight of an animal on the addition of meat extracts to an extractive—free diet. Some small part of this increase is no doubt due to the better digestion and assimilation of the foodstuffs as the result of the action of the extractives on the digestive juices, but by far the greater part of the increase is due to a water retaining faculty which they exert. This fact was discovered by Rubner. In other words, meat extracts have an anti-diuretic effect, which is just as well, considering the primary position of soup in a meal. The retained water is slowly excreted and the weight of the animal returns to normal shortly after the extractives are omitted from the diet. Apart from the metabolic action of meat extracts taken by the mouth, little or nothing is known. They certainly produce a feeling of well-being in a hungry person, but experimentally it has been shown (Slade) that they have no stimulant action on the central nervous system, nor do they increase the power of doing physical work as caffein and alcohol are known to do. When introduced directly into the circulation meat extract has definite effects such as lowering the blood pressure, and increasing the rate and activity of the heart in moderate doses. In larger doses it causes languor, prostration and symptoms characteristic of fatigue. None of these effects are produced by meat extracts taken by the mouth, largely, no doubt, because they are only slowly absorbed. At the same time it seems possible that meat extracts exert their fundamental action in consequence of being absorbed through the intestine, because of some reaction between the extractives and the intestinal mucous membrane.

To sum up, besides their important stimulating action on the digestive mechanism, extractive substances are an essential constituent of diet; they supply little or no energy to the body, but without them other foodstuffs cannot be utilised, and in growing animals growth stops and death results; when deficient in a diet pathological lesions may result.

Therapeutic Use.—No better indication of the requirements of a patient for meat extracts can be afforded than a desire for such substances, and it is but seldom that a convalescent patient, or one suffering from general weakness, does not appreciate meat extracts when other foods may be distasteful. Such an indication has often been abused by allowing soups and similar substances to be almost exclusively taken, and it cannot be too much emphasised that extractives supply little or no energy to the body but only aid the tissues to make fuller use of proteins, fats and carbohydrates.

One of the first results of all ill-health is a depressed state of the alimentary canal, both as regards the secretion of digestive juices and the movements, and meat extracts may bring about great improvement by stimulating a good flow of gastric juice, and, indirectly, other digestive juices. In convalescence, and after illnesses, which have produced emaciation, they are necessary for increasing the body weight and aiding tissue synthesis. Again, the desire of women after parturition for tasty foods is but an indication that the body needs an increased amount of extractives, probably to make up for those supplied to the child *in utero*.

Meat extracts when given in large quantities may produce diarrhœa, and such a result would naturally indicate a reduction in the quantity given.

The expressed juice of fresh meat is beneficial in cases of scurvy, and, recently, vitamine has been obtained from meat which is curative of experimental beri-beri in pigeons.

Malt Extract, U.S.P. (Extractum Malti)

Malt consists of barley which has been partially allowed to germinate and then dried. The extract of malt is made by allowing malt to be macerated and digested for an hour with water at a temperature not exceeding 55°. The solution is then evaporated in a vacuum at a similar temperature so that the diastatic ferment is not destroyed. In the course of this treatment the starch is largely digested by the enzyme to maltose. Malt extracts also contain nitrogenous substances whose constitution is unknown, some part being of a protein nature and some of simpler structure, and related to the extractives of other biological tissues such as have been previously mentioned.

It is a thick, viscid liquid, brown-yellow in colour, having a sweet mucilaginous taste and an acid reaction.

Malt extract has the following constitution [1]—

	Total Solid	Reducing[2] Sugars	Protein[3]	Dextrin	Ash	Diastatic Power
Maltine . .	67·3	61·9	5·25	5·0	1·2	940
Standard Extract of Malt . .	76·6	70·0	5·3	12·2	1·4	382

The three qualities of malt extracts which render them of therapeutic interest are—

1. They contain a large proportion of the end product of carbohydrate digestion, viz. maltose.
2. They contain, as a rule, diastatic ferment.
3. They contain the group of substances described as extractives.

Since maltose is further broken down to the monosaccharide dextrose before being absorbed into the blood stream, it is doubtful whether the first property would justify the use of this substance as a food drug, especially when its high price is considered. From the point of view of an energy supplier to the body 20 gm. of malt extract, *i. e.* a large tablespoonful has a heat value of 60 calories equivalent to that of an egg. The presence of the diastatic ferment may undoubtedly be an important adjuvant to the saliva and pancreatic juice in the preparation of starch for absorption.

The physiological action of extractives has been already fully considered, but it is interesting to note here that so long ago as 1777 an infusion of malt was strongly recommended by Forster, who accompanied Cook on his second voyage, as a cure for scurvy.

Therapeutics.—Extract of malt is given to children because of its nutritive value, but it is an expensive form of nutriment. It has the merit of being very palatable, and is taken with satisfaction by children. There is no doubt that badly nourished children often improve wonderfully when malt is added to the diet. If it is given in consequence of its diastatic qualities, it must be remembered that in many cases this ferment has been killed in manufacture or by its acid reaction. Many proprietary foodstuffs are malted, some before reaching the consumer, and so having the starch of the cereals already converted to maltose, and some containing the malt ferment.

Undoubtedly the greatest value of malt extract is due to its use as a vehicle, and more particularly in the administration of cod-liver oil (*see* Extractum Malti cum Oleo Morrhuæ). The cod-liver oil under such conditions is more easily taken, and it is possible that, just as the efficient combustion of fat in the body requires the presence of carbohydrate, so, it may be, the presence of the maltose increases the digestibility and assimilability of cod-liver oil.

The liquid extract of malt is also occasionally used as a vehicle with hæmoglobin, extract of cascara and hypophosphites.

The action of the nitrogenous extractive substances may also be important in disease (*e. g.* scurvy), and during convalescence, but there is no reason to believe that they are more efficacious than the cheaper extractives of other biological tissues.

Alcohol

The pharmacological and therapeutic action of alcohol has been dealt with elsewhere in this book, but in this chapter devoted to food drugs it might be well to consider this substance as a source of energy to the body.

Alcohol as a food has been the subject of much research and diverse results have been obtained, but this diversity may be explained to a large extent by the different conditions of the experiments, and a failure to realise that alcohol, when allowed to exert its immediate toxic influences, has a different metabolic effect than when given in small quantities over prolonged periods. The elaborate experiments of Atwater and Benedict are conclusive that alcohol is an easily assimilable foodstuff, and can replace isodynamic quantities of carbohydrates and fat in the diet. Some of their results are as follows—

INFLUENCE OF ALCOHOL ON METABOLISM

Duration of Experiment in days.	Grams of food. Protein.	Fat.	Carb.	Alcohol.	Calories in food.	Calories of Metabolism.	Protein balance.
13	114	69	354	0	2496	2221	− 2·0
10	115	47	273	72·2	2488	2221	− 3·8

[1] Robert Hutchinson's *Principles of Dietetics.* Further information on extract of malt, malted foodstuffs and meat extracts can be obtained from this book.
[2] Calculated as Maltose.
[3] The N calculated as protein, but this is misleading.

On the alcohol days, 500 calories were supplied in the 72 gm. of alcohol, *i. e.* a quantity of alcohol equivalent to a bottle of claret. It was administered in six small doses per diem, and 98 per cent. was completely burnt in the organism. On the ordinary days 33·7 gm. of fat were added to the body and on the alcohol days 34·1 gm. of fat.

It is frequently stated that the food value of alcohol is obvious from the obesity of the alcoholics, but this is not so demonstrative as it appears at first sight. In the first place the energy value of such an article as beer is by no means all due to the alcohol. A litre of German beer contains 3 to 4 per cent. alcohol and 5 to 6 per cent. extractives, and has a caloric value of 450, but only half of this energy is due to the alcohol. Again, the question of obesity is complex. It is not due to the fact that food of an increased caloric value is being ingested, but rather that the body fails to oxidise the increase of food. Consequently the fattening effect of alcohol may be due to any or all of three causes—

1. It can supply all its energy to the body and therefore save fat.
2. It may directly reduce the oxidising powers of the cells.
3. It may so act on the central nervous system, or the neuro-muscular mechanism, as to reduce the activity of the individual, and therefore reduce the oxidising processes.

The first action alone will not explain alcoholic obesity, and it seems probable that the third action, resulting in the change from an active condition to comparative lethargy, is the most important. Such a result one might expect from the inhibitory action of alcohol on the central nervous system, a fact which is now generally accepted.

Alcohol is, therefore, a food and a fat, carbohydrate and protein sparer, but a normal individual can only take 3–5 per cent. of the caloric value of a day's diet in the form of alcohol without experiencing intoxication.

One action of alcohol on the energy balance is of interest, namely, the increased loss of heat which immediately follows its access to the alimentary canal. Both in the alimentary canal and at the skin, alcohol produces a vaso-dilatation and the concomitant feeling of well-being, and this vaso-dilatation is responsible for the increased loss of heat. The loss of heat may be greater than the heat energy supplied in the alcohol to the body. It is this action, together with the general depression that follows the taking of alcohol, that explains why alcohol is forbidden in conditions of stress with no immediate prospect of food, as, for instance, when caught by a blizzard while mountaineering.

The question as to the conditions in which alcohol may be prescribed as a foodstuff is difficult, and each case must be considered on its merits. It is certainly of but little value as a food to a patient unaccustomed to alcohol because of the predominance of its toxic effects. In the case of a patient accustomed to alcohol, and therefore more resistant to its toxicity, it might be useful under certain conditions. For instance, such a patient suffering from typhoid fever, and capable of taking very little nourishment, would probably be able to make full use of its energy to sustain him, and at the same time experience no toxic action. Again, in some cases of diabetes alcohol has been shown to reduce the acetonuria and glucose excretion, and consequently it may be of value in such cases as a food.

Glucosum, B.P. ($C_6H_{12}O_6$)

Synonyms—Dextrose : Pure Grape Sugar.
Also met with as Glucosum Liquidum (B.P.C.).

Glucose is obtained by the inversion of starch by dilute acid.

It has recently become clear that, not only is carbohydrate essential to the organism for the katabolic changes of fats and the carrying out of protein synthesis from amino acids, but also the defensive mechanism of the body against toxic substances depends largely on its carbohydrate supply. This is specially clear when an otherwise lethal dose of thymotin piperidid is given to an animal together with glucose. In this case the poisonous substance loses some of its toxic effect. A similar inference is possible in the clinical observations of the susceptibility of the diabetic to infections, such as those producing boils, carbuncles, gangrene of the limbs and tuberculosis. The susceptibility also of fasting patients to post-operative chloroform poisoning is well recognised. How carbohydrates carry out the defence against toxins is not understood, but there can be little doubt that, in being the most easily available source of energy to a living cell, they increase the defensive mechanism of the cell. An additional explanation is that carbohydrate products as, for instance, glycuronic acid, combine directly with toxic substances, like camphor and benzol, and render them innocuous, and these observations may be of much wider application. Certain it is that the body loses its carbohydrate store quicker than any other in starvation and under toxic influences, and the maintenance of carbohydrate by administering glucose might be expected to be beneficial to the patient.

Therapeutic Use.—Glucose may be given with beneficial results in cases where, for any reason, ordinary carbohydrates cannot be taken by

the mouth. For instance, after operations, and more especially after abdominal operations, a solution of glucose may be usefully injected either subcutaneously or intravenously. In such cases a solution of 5 per cent. glucose which is isotonic with the blood is used. In order to inject it slowly, and at the body temperature, it is useful to place the solution in a vacuum flask. When injected subcutaneously, the axillary region is usually chosen. The drawback to subcutaneous injection is the difficulty of keeping everything aseptic, and an abscess frequently results. There is also some danger in the intravenous injection, and the rate of injection must be very slow because of a liability of producing œdema of the lungs. Glucose injected in severe cases is, however, of undoubted benefit. Large quantities are assimilated by the patient, and there is an immediate reduction of the acetonuria. Such cases are frequently treated by the rectal injection of glucose, but the absorption of glucose into the blood stream by this means is small, and there is very little reduction in the excretion of acetone. Glucose is also given in cases of delayed chloroform poisoning, by mouth if there is no vomiting, and subcutaneously or intravenously, if vomiting prevents alimentary absorption. Other conditions, in which glucose is usefully injected, are the toxæmias of pregnancy and the puerperium when no nutriment can be taken by mouth.

Glucose given by the mouth has a constipating effect, and this must be guarded against.

Levulose (B.P.C.) or Fructose

$C_6H_{12}O_6$, Lævorotatory. Isomeric with dextrose levulose is frequently found in nature, in honey and with grape sugar in fruits. Just as the hydrolysis of starch with dilute acids yields dextrose, so the hydrolysis of inulin, another constituent of plants, *e. g.* the tubers of dahlias, and having the formula $(C_6H_{10}O_5)_n$, yields levulose. It is readily soluble in water and dilute alcohol. Cane sugar is composed of equal quantities of dextrose and levulose, and before absorption from the alimentary canal into the blood stream it is split up by invertase of the intestinal juice into these substances. The body, normally, treats dextrose and levulose alike, and both are stored up in the liver as glycogen. Levulose is sometimes found as an abnormal constituent of urine.

Therapeutic Use.—Being a carbohydrate, levulose may be used in a similar way to, and on the same basis as, glucose. It is much sweeter than glucose and even than cane sugar, and is sometimes given in large quantities (4 to 8 oz. per diem) in wasting diseases of children.

Some cases of diabetes are said to be able to metabolise levulose when other carbohydrates pass through the body and are excreted as glucose. Consequently it has come to be used as a sweetening agent instead of cane sugar in diabetic cookery. It is said to be specially useful in warding off impending diabetic coma.

Lactose or Milk Sugar

Saccharum Lactis (B.P., U.S.P.), $C_{12}H_{22}O_{11}$, H_2O. Dextrorotary. When hydrolysed lactose yields dextrose and galactose, it is not fermentable.

It is sometimes found in the urine of suckling animals, and reduces Fehling's solution. Before absorption into the blood stream lactose is broken down by the lactose of succus entericus to dextrose and galactose. If this does not take place lactose is excreted unchanged, for the cells of the body are unable to use it.

Therapeutic Use.—The principal use of lactose is in the manufacture of humanised milk from cows' milk. Cows' milk is diluted with an equal quantity of lime water or barley water in order to reduce the caseinogen content, and lactose (one teaspoonful to every 4 oz.), and a similar quantity of cream are then added.

Changes affecting the lactose of milk are the basis of the formation of such remedies as koumiss, kephir and sour milk.

Koumiss is mare's milk which has been fermented, or rather, which has first been converted by lactose into dextrose and galactose, and further, fermentative changes allowed to go on. Kephir has a similar constitution to koumiss, but is made out of ordinary cow's milk. Lactic acid fermentation as well as alcoholic fermentation are allowed to proceed, but the former is suppressed as much as possible.

In the case of sour milk the lactose has been again changed, but here the lactic acid fermentation is more prominent than the alcoholic. This treatment of milk has become popularised in England by the work of Metchnihoff, who advocates souring by means of the Bulgarian bacillus. In this case, the bacilli are taken with the milk, the hypothesis being that this resistant organism becomes acclimatised to the intestinal canal, and by a continual production of lactic acid in the large intestine, prevents the formation of the well-known ptomaines from the amino acids of digestion. It is known that ptomaines such as β-imidazolethylamine and parahydroxy phenylethylamine are not formed from their respective amino-acids, histidin and tyrosin in the presence of acids. Sour milk has been advocated for many complaints, including neurasthenia and intestinal affections, colitis, diarrhœa and constipation, and those conditions, supposed to be due to alimentary toxæmias, such as gout and arterio-sclerosis.

Whatever the value of the treatment may be, and this seems to vary considerably in the hands of different people, it is to be regretted that it continues to rest on an empirical basis, and no adequate efforts have been made to see that the facts are in accordance with theory. That such is the case seems unlikely for the following reasons—

1. The presence of the Bulgarian bacillus in the large intestine would only be of value if carbohydrate were also there, so that acid could be produced. On the contrary, carbohydrate is rapidly absorbed from the small intestine, and is probably absent in the large intestine.

2. The presence of the bacillus in the small intestine is superfluous, for the reaction of the intestinal contents varies profoundly at different times and in different places in the intestine. In an inactive state the small intestine is normally acid, and when active digestion and absorption are going on, any acid produced by fermentation would be insignificant to the alkali of the succus entericus.

In considering sour milk treatment it has been customary to regard the intestine as an inactive coil of membrane, the real fact being that it is more reactive, and has greater powers of defence, than any other tissue of the body.

In its physiological effects lactose stands on a different plane from glucose and levulose. Little is known of this subject, but such a difference might be expected in the case of a substance containing a galactose moiety, for there are a large number of the lipoid substances in the body containing galactose, and although their function is not known, they are probably important.

Lactose seems to have a stimulating effect on the mammary gland secretion, and may often be given with advantage to nursing women. It is interesting to compare the effect of adding separately lactose and glucose (say 100 gm. per diem) to the diet of nursing women and comparing the progress of the children. The glucose has a most depressing effect on the mammary gland secretion, while this is not the case with the lactose-fed mothers.

Lactose is not very soluble and is best given with milk puddings which partly conceal its gritty nature.

Lecithin, Glycero-phosphates and Hypophosphites

Hypophosphites have been recommended in the treatment of phthisis, when they are said to improve the appetite and digestion, and to lessen the cough and expectoration. They are also said to be useful in anæmia and general weakness. Recently lecithin and glycero-phosphates have become popular substances in treatment, on the assumption that the phosphoric acid is more readily absorbed when attached to an organic radicle. This is a fallacy and depends on experiments which were not satisfactorily controlled. Plimmer has recently shown that all organic phosphoric compounds except phytic acid are readily acted upon by the intestinal ferments with the liberation of inorganic phosphates, so that it is almost certain that phosphoric acid is liberated from such before absorption. Again, Fingerling has shown that the animal body can synthesise organic phosphorus compounds from inorganic phosphorus compounds, for ducks fed on food containing only inorganic phosphorus over long periods laid approximately the same number of eggs with the same lecithin and nuclein content as other ducks which were given organic phosphorus compounds in the food.

The high price of lecithin and glycero-phosphate renders it necessary to point out that whatever beneficial action they have in abnormal conditions their phosphorus moiety is no better than the cheaper hypophosphites. Nothing is known as to the action of lecithin in the organism, and the beneficial effects following its ingestion are only matters of personal opinion, and do not appear to have been thoroughly tested by experiment. It is preferable to take it in the form of eggs than in the forms of proprietary medicines. Since lecithin is an important constituent of nervous tissue (non-medullated nerves contain 10 per cent. lecithin) it has been assumed that this substance improves the nutrition of the nervous system, and consequently it has been recommended for neurasthenia. It is also given in cases of anæmia and malnutrition. Lecithin is given by mouth as an emulsion (Emulsio Lecithini) and an elixir (Elixir Lecithini). With the object of escaping decomposition by ferments in the alimentary tract, lecithin is sometimes injected intra-muscularly together with sterilised olive oil.

Hypophosphites are given in the form of salts of sodium, potassium, calcium and iron, 3–10 gr.

Syrupus Hypophosphitum contains the hypophosphites of Ca, K, and Na together with free hypophosphorous acid.

E. M.

HORMONES AND FERMENTS

The so-called "organotherapy" or "opotherapy," the administration of animal tissues or extracts thereof, really includes two different kinds of treatment. In the first place the preparation may be given to replace a deficiency of the natural, internal secretion of the corresponding organ in the patient, when such deficiency is supposed to be the cause of the condition to be treated. The classical case is,

of course, the administration of thyreoid gland substance for cretinism or myxœdema. In the second place the active principles elaborated in two of the ductless glands, the suprarenal and pituitary glands, have an immediate, powerful pharmacological action, and preparations from these are used like the vegetable alkaloids, in symptomatic treatment, to produce a sudden and temporary exaggeration, either locally or on the system generally, of an action which the normal, steady output from the gland exerts only in a mild and imperceptible form. The experimental basis of this latter mode of employing certain animal principles is as good as that of any drug treatment, and better than that of most. The same can hardly be said for many of the applications of the other form of organotherapy, aiming at substitution for a deficient natural function. The brilliant results obtainable by administering thyreoid gland rank, indeed, among the best-established facts in the whole range of therapeutics. It must be remembered, however, that its success depends on several conditions. The thyreoid gland stores a large reserve of the substance, whose presence in the general circulation, in small amounts, is essential to the normal growth and function of many of the tissues. This principle is a highly stable substance; it resists drying and the action of the digestive juices, and, when administered by the mouth, is absorbed in sufficient quantity to maintain the action which the thyreoid gland normally produces, and thereby to replace a suppressed or deficient internal secretion from the gland. It is not too much to say that there is no certainty that any one of these conditions is realised in the case of any other organ of internal secretion. Such evidence as exists is rather in the other direction. The analogous pituitary deficiency, for example, is said to be somewhat alleviated by giving pituitary substance by the mouth, but only when relatively enormous quantities are ingested daily. It is possible that this and other glands secrete their essential product as fast as they form it, so that the gland never contains a large store of it. Or the active substance may be highly unstable; or so complex that its specific character is entirely destroyed by digestive cleavage. There is much room in this field for careful observation and experiment, and there are many conditions in which the sheer bankruptcy of other methods of treatment make this worthy of an intelligent trial. But there is no justification for its undiscriminating advocacy.

The Thyreoid and Parathyreoid Glands

The internal secretion of the thyreoid gland is essential to normal growth and function. Its defect in early life produces the characteristic dwarfish idiocy known as cretinism. Later in life an atrophic condition of the gland gives rise to the condition known as myxœdema. There are various conditions which are associated with a relative thyreoid defect, which may be roughly summarised as a general slowing of metabolism, leading to lethargy, excessive fat formation and slow intelligence. On the other hand there is much good evidence in favour of attributing to excessive thyreoid secretion the symptoms of exophthalmic goitre (Graves's or Basedow's disease), in which emotional and nervous instability, and general acceleration of metabolism, is associated with excessive excitability of structures innervated by the true sympathetic system, and with tremors of the skeletal muscles.

Experimentally thyreoid deficiency and over-activity can be reproduced by removing the gland or administering it in large quantities. The removal of the thyreoid in young herbivora, in which one pair of parathyreoids is situated at some distance, has been found to cause stunting of the growth and a vaguely cretinoid condition. In carnivora, on the other hand, the whole of the parathyreoid apparatus is removed with the thyreoid gland, unless special precautions are taken, and their loss is followed by a train of nervous symptoms, in which tetany is the predominating feature, and which are usually fatal in the course of a few days.

Administration of thyreoid gland to animals in large quantities causes a large increase in katabolism, so that the output of the nitrogen in the urine is largely increased, and weight is lost rapidly. The oxidation of fats is similarly accelerated. Nervous symptoms are also produced—muscular tremors, and, in some species, the characteristic staring exophthalmos of Graves's disease. An intolerance for sugar occurs, so that addition of carbohydrate to the diet readily leads to glycosuria.

The injection of thyreoid extract intravenously causes a fall of blood pressure, but this cannot be regarded as specific, since extracts from most glandular organs have the action in greater or less degree. An after-effect of such injection is said to be an increase in the response of plain muscle and gland cells to stimulation of sympathetic nerves or injection of adrenine. A similar increase has been described as the sequel to stimulation of nerves to the thyreoid gland. The bearing of these observations on certain features of Graves's disease, such as the accelerated heart-beat and exophthalmos, will be obvious.

The active constituent of the thyreoid gland is a complex protein containing a considerable proportion of iodine, the thyreoid being the only tissue in the higher animals which contains any quantity of this element. The chemical

structure of the grouping to which the iodine is attached has not been elucidated, but Baumann has shown that a relatively simple substance, containing over 9 per cent. of iodine, can be split off from thyreoid protein by acid hydrolysis. This "iodothyrin" cannot be regarded as a pure chemical substance, and its administration has not the same constant value as that of whole thyreoid substance.

There is some rather indirect evidence in favour of the view that the therapeutic activity of the thyreoid gland substance is proportional to its natural iodine content. Reid Hunt found that mice which were given thyreoid substance with the food developed an abnormal tolerance for acetonitrile, which is a powerful poison for normal mice. The degree of tolerance produced was proportional to the amount of iodine in the thyreoid ingested, but administration of iodine in other forms had no effect. It is not yet proven that this peculiar effect of thyreoid substance is due to the principle or principles which so profoundly influence normal metabolism; but there is sufficient presumption in favour of such a supposition to make it desirable that all thyreoid substance used in therapeutics should be standardised for iodine content, since considerable variations occur among the glands from animals fed under different conditions and therefore with change of food at different times of year.

The fact that removal of all the parathyreoid glands causes fatal tetany was mentioned above. This observation has led to the supposition that tetany, and various conditions of tremor, such as paralysis agitans, are associated with para-thyreoid deficiency. The evidence in favour of such a connection is rather vague at present.

Therapeutics.—Thyreoid medication is of specific value in myxœdema and cretinism. The injection of thyreoid extract in myxœdema was first tried by Murray, and his demonstration of its value was soon followed by the proof that oral administration of the gland substance had a like good effect. The dried substance in cachets or tablets is almost always employed now in such cases. The administration must be continued throughout life. Liquor Thyreoidei may also be used, but it is not a stable preparation and must be obtained fresh. An Extractum Thyreoidei Liquidum is made with a larger proportion of glycerin and is said to keep well.

Thyreoid administration should also be tried in cases of arrested growth and development where thyreoid deficiency is suspected. In such cases it may be possible to discontinue the treatment gradually as the thyreoid regains normal function. As an adjunct to dieting there is no remedy which so rapidly reduces excessive obesity as thyreoid substance. It must be remembered that it accelerates nitrogenous metabolism as well as fat-combustion, and the treatment should be carefully watched. Administration of iodine, which is in part taken up by the thyreoid, with the probable result that more of the active constituent is formed, is said to have a similar effect in minor degree. The use of the seaweed, fucus vesiculosus, which enters into the composition of several proprietary remedies for obesity, is to be explained by its iodine content. In cases of goitre, associated with symptoms of thyreoid deficiency, thyreoid substance may be given with benefit. In exophthalmic goitre, on the other hand, where the secretion is already in excess, it is contra-indicated. There are numerous other conditions in which thyreoid treatment has been recommended on less scientific grounds. It must be remembered that the thyreoid gland of the sheep, from which the official preparations are made, contains the substance of the internal parathyreoid distributed among its alveoli; so that some of the applications of thyreoid, which are reputed to be valuable, may find their rational explanation when the physiology of the parathyreoids is better elucidated. Among effects not improbably of this kind may be mentioned that in puerperal eclampsia, in which condition the injection of thyreoid extract is said to be sometimes of great benefit. Any beneficial effect of thyreoid in tetany must also be attributed rather to the parathyreoid which it contains.

Preparations

Thyroideum Siccum (B.P.). ½–4 gr. (3–25 cg.).

Glandulæ Thyroideæ Siccæ (U.S.P.). 4 gr. (25 cg.).

Liquor Thyroidei (B.P., 1898). 5–15 min (3–10 dl.).

Extractum Thyroidei Liquidum (B.P.C.). 5–15 min. (3–10 dl.).

Tabellæ Thyroidei (B.P.C.). 2 gr. *Dose:* 1–5.

The Pituitary Body (*Hypophysis Cerebri*)

This gland consists of an anterior, glandular or hypophyseal lobe, a posterior, nervous or infundibular lobe, and an intermediate portion or pars intermedia. The functional relation of these different portions is not definitely established. It is quite certain, however, that the potent active principle yielded by the gland, and having an immediate, recognisable physiological action of great intensity, is contained in the posterior, or infundibular, lobe. Pathological conditions affecting the anterior lobe, and modifying its action in the direction of excessive or deficient activity, seem to be

responsible for the conditions of acromegaly and gigantism on the one hand, and of a peculiar obese infantilism on the other. There is no evidence of connection between these two types of action, which may be dealt with separately.

Immediate Physiological Action : Infundibular Lobe.—The action of extracts of the pituitary body, like that of the suprarenal glands, was discovered by Schäfer and Oliver, who found that it had a powerful pressor action, due to vaso-constriction almost entirely. The heart-beat is, indeed, strengthened, but its rhythm is concurrently retarded, the action being not unlike that of the earliest stages of digitalis action. Later Schäfer, with other co-workers, described the powerful diuretic action of the extract. Ott found that it caused secretion of milk, and this galactogogue action has been confirmed by Schäfer and Mackenzie. Dale showed that the plain muscle of the uterine wall is extremely responsive to the action of the extract, and Blair Bell and Hick were the first to record a stimulant action on the bowel of the rabbit, which is not seen in carnivora, but forms a prominent feature of the action on man.

The effects on involuntary muscle have no apparent relation to innervation by one or other division of the autonomic system, and they are unaffected by the action of poisons, such as ergotoxine, which annul or profoundly modify the action of adrenine. According to some observers the vessels of the kidney are exceptional in being dilated by the action of the extract, and experiments with isolated strips of arterial wall have shown a variable reaction in the arteries of the splanchnic area generally. But there is no relation of the effects to innervation, nor any reason for supposing that the extract acts otherwise than directly on the plain muscle fibres.

Whether the various effects are produced by one or by several principles is still a matter of uncertainty. Of the chemical nature of the active constituent, it is only known that it is basic, highly soluble in water, hardly at all in alcohol. Several crystalline substances, exhibiting the action in varying degrees, have been described, but further evidence of their purity and nature is needed. All the activities of the extract are readily destroyed by tryptic digestion, and the diuresis recorded as the result of feeding with the gland must be due to absorption from the stomach.

Therapeutic Uses.—Extracts from the infundibular lobe of the ox are used chiefly for three purposes—

1. To raise the blood pressure, by producing general arterial tone, and indirectly strengthening the heart-beat, in shock and collapse. Especially in preventing shock after prolonged and severe operations, and in relieving collapse after serious loss of blood, or after prolonged and difficult labour, such an extract has proved of great value.

2. To restore activity to the bowel in the condition of paralytic distension following abdominal operations. Infundibular extract is the only remedy of proved value in this condition.

3. To promote contraction of the atonic uterus. This was the first of the effects of the extract to find clinical application, and is the most widely used. In this country it is not usually administered until the third stage of labour is completed, but many authorities, especially in Germany, freely advocate its employment in the earlier stages, when the uterus shows deficient activity. Certain recently reported cases, in which death of the fœtus and rupture of the uterus were produced, will probably give a check to the general adoption of this procedure. The extract has an advantage over ergot in its freedom from toxicity in ordinary doses, the general effects being, indeed, a useful adjunct to those on the uterus; unless mechanical obstruction exists there seems little danger of giving an overdose.

One other point in its physiological action is of practical interest. When a maximal dose has been given further doses have practically no effect for a few hours. It is useless, therefore, to repeat injections at frequent intervals.

The diuretic and galactogogue effects have not been much applied as yet, but should be worth a trial at least.

The Action of the Gland on General Metabolism.—The success of thyreoid treatment naturally suggests the administration of pituitary gland substance in cases of subpituitarism. Cushing has reported good results from the daily administration of as many as 50 glands from the ox. It is evident that comparatively few patients could be treated on such lines. An experiment should be made with the separated hypophyseal or anterior lobes, large quantities of which must be obtainable, now that the infundibular extract is used on such a large scale.

Preparations

No pharmacopœia yet includes the pituitary gland or any extract therefrom. The extracts of infundibular lobe in common use are watery decoctions of the fresh substance, the strength most employed being a 20 per cent. extract of the fresh, moist substance. The extract loses activity very rapidly if organisms grow in it. It must be preserved by heat sterilisation in sealed bulbs, or by addition of some antiseptic.

The Suprarenal Glands

The action of the active hormone, adrenalin, has been dealt with elsewhere. Substitutive

administration has not been successful in the case of the suprarenal gland. The substance of the whole gland will doubtless continue to be used in Addison's disease, until some really effective treatment for the condition has been discovered. Neither the gland nor its active principle, administered in any quantity or by any method, has proved to be capable of doing more than to postpone the fatal issue.

Preparations

Adrenalinum (B.P.).
Liquor Adrenalini Hydrochloricus (B.P.).
1 in 1000. *Dose:* 10–30 min. (6–18 dl.).

Other Ductless Glands

The use of other ductless glands is on a much more doubtful basis. Mention should be made of the administration of ovarian and testicular substance, since the conception of organotherapy may be said to have originated with Brown-Séquard's attempts to renew his youthful vigour by injecting testicular extracts. There is evidence connecting the internal secretion of the corpus luteum with the suppression of menstrual activity and the growth of the mammary gland during pregnancy. Preparations from the (false) corpora lutea of the sheep's ovary are said to be of value in threatened abortion. The effect of ovary and testis, given by the mouth, in controlling the nervous symptoms of the menopause, in hysteria or in neurasthenia, may be a genuine hormone action, or may be the result of suggestion. The thymus gland was formerly administered in Graves's disease, but there seems no good evidence of its value or rational basis for the treatment. The administration of pancreatic substance or extracts in diabetes has been a complete failure; the gland probably forms the hormone controlling carbohydrate metabolism continuously, and without storing any quantity at one time. Some years ago secretin, the hormone from the duodenum which excites pancreatic secretion, was tried in diabetes, on the theory that the disease might be due to lack of adequate stimulus, rather than to permanent loss of function of the gland. After a temporary vogue this also proved to be without definite effect.

Although it cannot be related on any theory to hormone action, mention should be made here of the administration of bone marrow, and especially red marrow, in anæmia. The practice would be difficult to justify on theoretical grounds. The hæmopoietic function of the red marrow is well established. But there seems no reason for regarding it as deficient in the cases which administration of marrow appears to benefit, or for supposing that the marrow of other species, taken by the mouth, could help such deficiency if it existed. The sanction for the treatment is, therefore, purely empirical. The fresh red marrow of oxen or sheep may be given, spread upon bread-and-butter. Various proprietary preparations are also available.

Ferments (Enzymes)

Though practically every organ and tissue of the body contains intracellular enzymes, which undoubtedly play an essential rôle in most, if not all, vital phenomena, the only enzymes which need practical consideration from the therapeutic point of view are those secreted into the alimentary canal in the digestive juices.

These, or their like, can be obtained in most cases in relatively stable form, and their use is based on the simple and obvious principle of replacing a pathologically deficient enzyme by introducing one from outside.

To replace the amylolytic ferments of the saliva or pancreatic juice, when these are supposed to be deficient, various diastases of vegetable origin may be employed, the commonest being malt-diastase, which should be present in properly prepared malt extracts, and which enters into the composition of many foods containing starch, and intended for consumption by the very young, or the enfeebled and aged. The digestion may be allowed to proceed *in vitro*, before the food is taken. When diastase is given by the mouth, with a meal rich in carbohydrates, its digestive action may be supposed to go on in the stomach, like that of the normal salivary diastase, until the gastric contents have become sufficiently acid to inhibit its activity.

Pepsin, obtained from the stomach of the pig, is also used for the predigestion of proteins, or for administration by the mouth with a meal, to assist the action of a defective gastric secretion. Its possible value is clearly dependent on the correct diagnosis of the condition, as due to lack of pepsin in the secretion. When the secretion is deficient as a whole, diluted hydrochloric acid is given with the pepsin.

The pancreatic ferments are used less for internal administration than the others, owing to the relative difficulty of diagnosing a pancreatic dyspepsia, and of ensuring that the ferments reach the site of their proposed action in active condition, since they are rapidly destroyed by the gastric juice. The preparation known as pancreatin, containing the mixed ferments, is, therefore, given several hours after a meal, being often enclosed in cachets with sodium bicarbonate. Another method of protecting the pancreatic ferments from destruction in the stomach is to enclose them in a capsule of some material which is not digested till the intestine is reached, such

as formalised gelatin, keratin, or salicin; but it must be admitted that there is no clear experimental evidence as to the success of these various precautions in securing the liberation of active ferments at the desired spot. It should be remembered also that defective digestion of fats is probably more often due to lack of the adjuvant bile than of the essential pancreatic lipase, and that in such cases bile should be given.

Both pepsin and pancreatin are more often used for the predigestion of foods than for direct administration. The latter is especially employed in the preparation of the so-called nutrient enemata. The tendency of recent evidence is to indicate that proteins, however far digested, are not perceptibly absorbed from the rectum, and that the usual nutrient enemata simply provide a culture-medium for putrefactive organisms; so that the harm which they do by irritating the bowel outweighs any nutritional value which they possess.

It would be obviously more rational, if it were possible, to stimulate the digestive glands of the patient to due activity by administering the appropriate hormone. Unfortunately the best-known body of the class, the pancreatic stimulant "secretin," can be shown experimentally to have but a weak effect when given hypodermically, and none at all when given by the alimentary canal, which would be the only practicable method for therapeutic administration.

Materia Medica and Preparations

Pepsinum (B.P., U.S.P). 5–10 gr.(3–6 dg.).
Glycerinum Pepsini (B.P.). 1–2 fl. dr. (4–8 ml.).
Liquor Pancreatis (B.P.). 1–2 fl. dr. (4–8 ml.).
Extractum Malti (B.P.C.). 1–4 fl. dr. (4–15 ml.).

H. H. D.

ANIMAL SERUMS

The article on *Specific Therapy* (Part I, p. 56) deals with the theory of the action of vaccines and immune serums, and the varying indications for their use. The use of animal serums, as being among the most important constituents of the animal body finding therapeutic application, may here be considered from a somewhat different aspect.

Normal Serum.—The serum of normal animals, especially when quite fresh, is credited with therapeutic value. The serum of the horse is generally employed, as being the one most easily obtained sterile in quantity. The indications for its use depend on the facts that it promotes coagulation of the blood, inhibits bacterial growth, and has an antitryptic action. The presence of fibrin ferment in fresh serum has led to its use by injection in cases of internal hæmorrhage, purpura, etc., dependent on defective coagulation. When the bleeding point or surface is accessible local application of the serum is the more rational procedure. The presence of normal antibodies to various bacteria in fresh serum has led to its application as a dressing to unhealthy granulations. It appears, when thus locally applied, to assist in clearing up a chronic suppuration.

To its antitryptic action has been attributed its effect in promoting the healing of chronic ulcers. It is applied on lint to superficial ulcers, or given by the mouth for gastric ulceration. It is supposed to inhibit the destructive action of the tryptic enzyme of pus cells.

Immune Serums.—These are obtained by the injection into animals of specific protein poisons, mostly of bacterial origin, to which the animal organism responds by the formation of "antibodies." The animal chosen is, in almost all cases, the horse, on account of the ease with which serum can be obtained from this animal in large quantities, under sterile conditions, and the relative freedom of horse serum from toxic action on most patients, as compared with that of some other species.

The article on *Specific Therapy* deals with the "antibacterial" and "antitoxic" serums, produced by immunising horses against bacillary substance, on the one hand, or against the soluble toxins formed in artificial culture by certain bacilli, such as those of diphtheria and tetanus, on the other. There are other protein poisons, however, such as those formed in the poison-glands of snakes and scorpions, or the protein of certain grass-pollens, which share with the soluble bacterial toxins the property of acting as "antigens." That is to say, their injection into an animal is followed by the appearance in its blood of neutralising substances, or antitoxins.

Antivenene.—When a non-fatal dose of a venom from a snake or scorpion is injected into a horse, the subsidence of the symptoms which it produces is accompanied by the appearance in the blood of antitoxic substances in excess; so that, by repeated graded injections, the animal can be immunised against the effect of many normally fatal doses.

The blood serum of such an animal is then found to be capable of neutralising considerable quantities of the venom, when the two are mixed *in vitro*. When injected into a normal animal such a serum confers a temporary passive immunity to the poison, and is even capable of saving the life of an animal which has received a fatal dose, if it is subsequently injected in sufficient quantity. Various such "antivenenes" have been produced by the immunisation of animals, usually horses, against the venoms of different snakes or of scorpions.

There is no doubt that, if the appropriate serum can be administered in sufficient quantity soon after the patient has been bitten or stung, so that the antitoxin is circulating in his blood before absorption of the poison has progressed far, an otherwise fatal issue can be prevented. There are several points which must be kept in mind, if there is to be a chance of success. Everything depends on getting the antibody into the circulation before the poison. The absorption of the latter, therefore, must be restricted, by ligature of the bitten limb, free incision with suction, or excision of the tissues round the minute wound made by the fangs, and other local treatment of the same kind. Meanwhile the serum should be made ready for injection at the earliest possible moment. Intravenous injection should be the method whenever possible, and, failing that, intramuscular injection. Large doses—50 to 100 c.c.—are essential for success in serious cases.

The venoms of snakes belonging to one zoological family have a certain degree of community in antigenic properties, but those of different families produce different antibodies. Success depends on the use of an antiserum containing antitoxin for the venom implicated. In districts, therefore, where venomous snakes of different families are found, it is important to have an antivenene prepared by immunising the horse against all the types of venom represented in the Ophidian fauna of the district. In India, for example, where the cobra and Russell viper are the principal poisonous snakes, an antivenene should be used from a horse immunised against a colubrine and a viperine venom.

Antiserum for Grass-pollen.—The protein of grass-pollen cannot be regarded as a toxic substance in itself, since most persons are not perceptibly affected by moderate doses. Not a few, however, show an abnormal sensitiveness to pollen, the presence of which in the air, during the months of middle summer, causes, in such subjects, the inflammatory reaction of exposed mucous membranes known as "hay-fever" or "hay-asthma." This specific sensitiveness has many points of similarity with the rarer sensitiveness to the exhalations of certain animals, to minute quantities of egg-albumin, etc. All such conditions have an affinity, as yet incompletely defined, with the acquired sensitiveness to foreign proteins known as "anaphylaxis."

Since pollen protein has antigenic properties, it is possible to treat hay-fever along either of the two main lines of specific therapy. The patient may himself be immunised, by injection of graduated doses of the pollen-protein, or the serum from an animal, brought to a high level of immunity by a course of injections, may be applied to the affected mucous membranes. Dunbar has prepared such a serum from rabbits and horses, and it is available in liquid form, as a dry powder, as a salve, or in pastilles. The liquid serum, powder or salve is applied to the mucous membrane of the conjunctiva and naso-pharynx before the attack for the day is due. Later, if symptoms develop, the application is repeated. Opinions are divided as yet as to the relative merits of this treatment and of active immunisation. The pollen-protein used for the latter is obtained by suspending the pollen of the Timothy-grass in water, freezing and thawing repeatedly, and evaporating the solution obtained at a low temperature. Apparently the effects of the immunisation are not permanent, the course needing yearly repetition.

Methods of Administering Serums.—Some cases are mentioned above in which certain serums are applied locally. To these may be added cases where a locally formed or injected toxin may be neutralised by local application of the appropriate antiserum. Thus dirty wounds, in countries where tetanus is common, may be treated prophylactically by dusting with dried tetanus antitoxin serum, as an additional precaution to the hypodermic injection of a prophylactic dose. It would seem reasonable similarly to supplement the injection of antivenene for snake-bite, by local application of the serum to the wound after free incision.

In the vast majority of cases, however, serums are given so as to act after absorption into the general circulation. The method most generally employed for administration is hypodermic injection; but it is more than doubtful if it deserves such preference. Experiment shows that an antitoxin hypodermically injected reaches the blood but slowly, so that the antitoxic content of the circulating blood reaches its maximum only after forty-eight hours. When it is remembered that the efficacy of antitoxin in diphtheria decreases with great rapidity as the disease advances, the desirability of reducing this delay needs no emphasis. For this reason intramuscular injection, which secures a much more rapid absorption, is to be recommended for diphtheria antitoxin in all but the earliest cases of diphtheria. For the same reason a large dose given early has much greater efficacy than the same quantity divided into smaller doses and spread over several days. In the matter of dosage the practice in Britain and on the Continent of Europe has been much more cautious and conservative than that in the United States of America and the British Colonies, where the injection of 100,000 antitoxic units is not uncommon in severe cases.

For prophylactic injections of either tetanus or diphtheria antitoxin the hypodermic method is the obvious one. When symptoms of tetanus have developed, large doses of the antitoxin intravenously or intradurally offer the only hope of a specific therapeutic effect.

As described under *Specific Therapy*, injection into the spinal theca has given much better results than other methods, in the use of antimeningococcus serum for cerebro-spinal meningitis.

Oral and rectal administration of immune serums find their advocates from time to time, but the whole weight of experimental evidence is against the view that they have any efficacy at all comparable with that of injection into the tissues.

Toxic Effects of Serums.—All serums are liable to produce certain toxic effects, which are quite independent of their antitoxic or antibacterial value, and which are as a rule of little practical significance. Three types of toxic phenomena may be mentioned.

1. *Primary Toxicity.*—Serums have some degree of primary toxic effect. This, as a rule, is only perceptible when the serum is given intravenously, is at a maximum soon after the serum is separated from the clot, and is rarely of serious import. The symptoms consist of circulatory depression and often some dyspnœa. In asthmatics the symptoms may be serious and even dangerous. The precautions to be observed are not to use serums which are too fresh—a fortnight after separation is given by some French authorities as the earliest date for use; to restrict intravenous injection to urgent cases; and to proceed with special caution in the serum-treatment of asthmatics.

2. *Delayed Toxicity.*—In a certain proportion of patients (usually about 20 to 30 per cent.) an injection of serum is followed, at an interval of about eight to twelve days, by a reaction, usually taking the form of an urticaria, but sometimes complicated with joint-pains, facial œdema, etc. The interval is suggestively similar to that necessary for sensitisation, and it may be that the symptoms represent an interaction between newly-formed antibody to the foreign protein, and traces of the latter still remaining in the circulation. The symptoms may be unpleasant, but are rarely serious. It is stated that they may be mitigated by administration of calcium salts, of which the lactate is the pleasantest to take. It appears to be well demonstrated, also, that the concentrated solutions of antitoxic globulins, separated from the whole serum by salt-precipitation, are less liable to produce these symptoms than the natural serum in doses of equal antitoxic content.

3. *Anaphylaxis.*—This specific sensitiveness, which is exhibited by a certain number of those who have been recipients of serum injections on a previous occasion, has been the subject of an enormous amount of research in recent years. It can hardly be doubted that the study of the symptoms in the guinea-pig, which presents the phenomenon with such regularity, and responds to a second injection with symptoms of such explosive violence, has tended to awaken a somewhat excessive alarm of its occurrence in man. At the same time it must be borne in mind that a fair proportion of those who have previously had serum injections show the condition in some degree, and that, in any such, the intravenous or intraspinal injection of a large dose of serum may have serious consequences. The symptoms presented are circulatory collapse, vomiting, dyspnœa and prolonged prostration. Several fatal cases have been recorded. When it is necessary to give an intravenous or intraspinal injection to a patient who has had previous serum treatment, the process of desensitisation, as described under *Specific Therapy*, is a wise precaution. Even with hypodermic injection severe symptoms, coming on within an hour or two of injection, are seen in a certain number of these cases. Some of the worst recorded have occurred in cases of prophylactic injections into healthy persons exposed to infection, and the wisdom of thus repeating prophylactic injections may be doubted. When serum treatment is called for the possibility of anaphylaxis is hardly sufficient to act as a contra-indication. It is an index rather for caution. When it is necessary to give serum intravenously in such cases, it should be diluted largely with warm saline, and run in very slowly at first.

When a course of serum injections is given, these should follow one another at intervals of not more than three or four days, so that each injection is given before sensitisation has resulted from the previous one. H. H. D.

ANTHELMINTICS

Male Fern, Pomegranate, Santonin, Thymol

For the treatment of intestinal worms the ideal drug would be one which, though harmless to the host, would act specifically on the parasite and kill it. Such a substance with an assured action is not yet known, so that it is necessary to choose one which kills or temporarily paralyses the worm and renders it more easily dislodged by purgatives, and at the same time is so slowly absorbed that it does not reach the tissues of the host in quantity sufficient to damage them.

In every case it is desirable that the intes-

tines should be as empty as possible before the anthelmintic is administered, in order that the drug may readily come into contact with the worm. With this end in view the course of treatment consists of a light diet with free purgation for one or more days, and on the last nothing but fluid is taken after midday. A purgative having been given overnight the anthelmintic is administered in the morning on an empty stomach, and is followed after an hour or two by another purge.

Certain essential oils and other substances have been used extensively in virtue of their antiseptic properties, but for the most part they cause intestinal irritation. Turpentine in full doses (3–4 fl. dr., 12–15 ml.) is of some value, and naphthol and thymol have been used with much success. In the treatment of ankylostomiasis thymol in large doses (15–30 gr., 1–2 gm.) is particularly indicated in conjunction with the usual course of purgatives, as mentioned above. In recent years papain has been administered with the object of digesting the worm *in situ* and thus killing it, and the treatment has met with some success. Its use depends on the fact that certain worms, especially ascaris, contain an antibody which neutralises the trypsin of the pancreatic juice and thus protect themselves. Papain is not so neutralised and consequently is able to attack the worm and digest it. This is the nearest approach to a specific therapy so far attained. It is important that the papain should be tested and its digestive activity proved; failure has often been due to the use of an inactive preparation from the neglect of this precaution.

The anthelmintics may be divided into groups according to the parasites for which they are chiefly used.

Tapeworm	*Round Worm*	*Ankylostomum*	*Threadworm*
Male Fern	Santonin	Thymol	Santonin
Pomegranate	Naphthalene	Male Fern	Thymol
Cusso			Quassia
Turpentine			
Papain			

Male Fern (Aspidium filix mas), is the best known of a number of ferns which have been used as anthelmintics. Several substances such as Filicic Acid, Aspidinin and Filmaron have been obtained from the oleoresin. Each of these has been credited in turn with special activity, but it is probable that the efficacy of the crude drug is due to a combination of these bodies together with others not yet isolated. In practice it is usual to administer the oleoresin obtained by extraction of the drug with acetone or ether. As a general rule it passes through the intestine unaltered and is not absorbed and causes no symptoms of any kind. Occasionally, and chiefly when large doses have been given, there may be evidence of intestinal irritation, with griping. Should absorption occur there may be vomiting, acute abdominal pain, muscular weakness and even convulsions, followed by coma and death; occasionally temporary blindness is observed. In some cases slight jaundice occurs, possibly the result of duodenal catarrh produced by the irritant action of the drug.

In animals similar symptoms have been produced; the intestinal congestion is due to the local action of the drug, whilst the twitching and convulsions are the result of its action on the spinal medulla. Death is usually the consequence of paralysis of the respiratory centre, though the heart muscle is also depressed.

The preparations of male fern are exceedingly unpalatable; the liquid extract is best administered in gelatin capsules, each containing 10–15 min., which can be swallowed whole. An emulsion can be obtained with acacia or tragacanth or with quillaia, and the mixture can be flavoured with ginger or oil of cinnamon.

Therapeutics.—The sole purpose for which male fern is used in medicine is the treatment of tapeworm and ankylostomiasis. Previous to its exhibition the bowels should be emptied by light diet and purgation. The drug is then administered, the total dose being given in two or more portions at intervals during a period of an hour. After one or two hours a purgative is again administered in order to cause the expulsion of the worm. The nature of the purgatives is not of great importance, a mixture of magnesium sulphate and senna is usually employed. Some authorities are strongly opposed to the use of castor oil on the ground that its solvent action on the oleoresin favours its absorption and the production of toxic symptoms. Others hold that it enables the drug to come into more intimate contact with the parasite and thus increases the efficiency of its action.

In spite of the risk of producing absorption, oily purgatives are frequently employed in practice, but it is noteworthy that in many instances of poisoning castor oil has been used. Toxic symptoms are most commonly found in anæmic and debilitated subjects; in consequence care should be exercised in prescribing it to these patients.

Should the treatment be unsuccessful and the head of the worm be not dislodged it is necessary to wait a few days or better a week before another attempt is made.

Poisonous symptoms are treated by washing out the stomach, administration of copious draughts of water containing saline purgatives to wash the drug from the intestine. Stimulants should be administered if necessary. Alcohol should be avoided.

Preparations

Extractum Filicis Liquidum (B.P.). 45–90 min. (3–6 ml.). An ethereal extract.

Oleoresina Aspidii (U.S.P.). 30 gr. (2 gm.). An acetone extract.

Pomegranate, Pelletierine. — Preparations of Pomegranate bark are of value as anthelmintics in virtue of their contained alkaloids. The chief are Pelletierine or Punicine, and Isopelletierine, which are closely related. At ordinary temperatures they are liquids and volatile, they are present to the extent of 0·5–1 per cent. The bark also contains about 25 per cent. of tannic acid, which renders its preparations exceedingly astringent and bitter. Pelletierine and its allies are specific for tapeworms, the movements of which are inhibited after six minutes' immersion in a solution of 1 in 10,000, while ten minutes' immersion is sufficient to cause their death; other intestinal worms are almost unaffected even by strong solutions.

In man, if absorption takes place toxic symptoms may occur; the commonest are weakness of the limbs, giddiness and confusion. Abdominal pain, nausea and vomiting may be present, but more rarely; these symptoms are probably due to the irritant action of the large quantity of tannic acid present.

The drug may be prescribed in the form of a decoction which, however, is very unpleasant to take owing to the large amount of tannic acid which it contains. The dose diluted to half a pint is administered, after the usual preparatory treatment, in two or more portions at intervals of an hour, and is followed by a brisk purge. The bark from which the decoction is prepared should not be too old, for the alkaloids tend to decompose on keeping. Owing to the unpleasant taste of the decoction it is generally preferred to prescribe the active principles in the form of pelletierine tannate. The alkaloids themselves or their hydrochlorides or sulphates are not often employed, for their greater solubility renders the production of toxic symptoms more likely. The tannate is given suspended in water in a manner similar to that described above.

Preparations

Fluidextractum Granati (U.S.P.). 30 min. (2 ml.).

Pelletierinæ Tannas. A mixture of the tannates of the pomegranate alkaloids. 2–8 gr. (12–50 cg.).

Santonin is derived from the dried unexpanded flower-heads of Artemisia maritima, in which it occurs to the extent of 2–3 per cent. It is a neutral substance, the lactone or internal anhydride of santoninic acid, into which it can be converted by treatment with alkalies; it is a naphthalene derivative. Santonin is insoluble in water, but soluble in alkalies and in oils.

On exposure to light santonin becomes tinged yellow, when it is said to be less poisonous, and is preferred for some purposes, such as the treatment of sprue.

In the stomach santonin is dissolved to some extent and some absorption takes place, but most of it passes on into the intestine. Occasionally the greater proportion appears to be absorbed from the stomach and the worms are not dislodged although toxic symptoms are produced. Some absorption always occurs from the intestine, for the urine is coloured golden yellow or red, according to whether its reaction is acid or alkaline. Disturbances of colour vision are almost invariably found; in the earlier stages objects appear bluish, but this is only transitory and is succeeded by a longer period in which yellow vision is the predominant feature. When large quantities have been taken the violet end of the spectrum is considerably shortened and blue and purple objects may appear black, while the sensitiveness to yellow is increased. These symptoms seldom last more than a few hours, though there may be a later transitory stage in which violet vision is in evidence. Formerly it was thought that the yellow vision was the result of staining of the media of the eye, but this view is unable to account for the other phases of the visual disturbance. It is far more probable that they are all due to the action of the drug on the retina or the visual centres of the brain. That santonin is a cerebral excitant is shown by the production of twitchings and convulsions when poisonous doses are given to an animal. In such cases death is due to failure of respiration during a convulsion; the circulatory system is not affected.

Santonin is extensively used in the treatment of round worm and threadworm. The worms are not killed inside the body, but the drug acts upon them in some way, causing them to release their hold so that the peristaltic movements are able to drive them into the large intestine, from which they are expelled by the action of a purgative.

Santonin is employed chiefly in the treatment of round worms (Ascaris), though in association with quassia and salt enemata it is also largely used for threadworms. It has little or no action on tapeworms. For children the lozenges are valuable, but a mixture in which santonin is suspended in an emulsion of castor oil is largely employed. Here, as in the case of male fern, there is a divergence of views as to whether oily emulsions are safe, for it is urged that toxic amounts are more readily absorbed from the intestine.

In order to mask the visual disturbance, it is advisable to administer santonin in the evening. The dose should be preceded by a light diet and laxative, and should be followed by a brisk purge at an interval of a few hours. Many prefer to administer santonin in the form of powder, combined with compound scammony powder (2 gr.), and calomel (½–1 gr.). The dose may be repeated on two or three successive days.

In the treatment of threadworms a mercurial ointment should be applied to the anus to kill eggs and allay irritation, and thus to prevent reinfection by the mouth from the fingers as a result of scratching.

Poisoning.—Should poisonous symptoms occur the stomach and intestines should be rapidly emptied by the stomach tube, purgatives and enemata. Anæsthetics may be necessary to stop convulsions. Disturbances of vision need no special treatment, for they are almost inevitable consequences of the administration of the drug and occur in a high percentage of cases.

Preparations

Santoninum (B.B., U.S.P.).
Dose : 1–3 gr. (6–20 cg.).
Trochisus Santonini (B.P.). 1 gr. in each.
Tablettæ Santonini Compositæ (B.P.C.). Santonin 1 gr. and calomel 1 gr. in each.
Trochisci Santonini (U.S.P.). ½ gr. in each.

Thymol or isopropylmetacresol is a colourless crystalline body derived from essential oil of thyme and other plants. It is but sparingly soluble in water (1 in 1,500), but very soluble in alcohol, ether and other organic solvents. It is used chiefly for its high antiseptic value. Its general action is similar to that of carbolic acid, but owing to its insolubility it is much less readily absorbed and hence less prone to produce toxic effects. Thymol is much used as a pleasant antiseptic for mouth-washes, gargles, etc. When rubbed with menthol, camphor or phenol it liquefies and a preparation consisting of thymol 1, menthol 1, chloral hydrate 1, and camphor 3, is much used as a mildly counter-irritant and analgesic paint. When absorbed in poisonous quantities it produces less cerebral irritation than carbolic acid, and tremors and convulsions are absent or less marked. An animal becomes apathetic and listless and ultimately dies. In fatal cases intestinal irritation and fatty changes in the liver are found. Thymol is excreted in the urine, some as organic sulphate, some unchanged and some oxidised to thymol-hydroquinone. During its excretion it may cause irritation of the kidneys with the appearance of albumin and blood in the urine.

Preparations

Thymol (B.P., U.S.P.).
Dose : ½–2 gr. (3–12 cg.) or more. As an anthelmintic 15–30 gr. (1–2 gm.) repeated.
Glycerinum Thymolis Compositum (B.P.C.). Contains 0·05 per cent. Is diluted 2–5 times and used as a spray for nose and throat or as a gargle.
Liquor Antisepticus (U.S.P.). Similar to the next preparation, but contains 25 per cent. of alcohol.
Liquor Thymolis Compositus (B.P.C.). Contains 0·1 per cent. thymol together with benzoic acid, eucalyptol, etc. When diluted 3–4 times is used as throat spray, gargle or skin lotion. May be taken internally for flatulence.
Dose : ½–2 fl. dr. (2–8 ml.)
Pastillus Thymol (B.P.C.). $\frac{1}{32}$ gr. in each.
Unguentum Thymolis Compositum (B.P.C.). 1 in 8 of thymol.
Unguentum Thymolis Compositum Dilutum (B.P.C.). Contains 1 in 3 of the above.

Therapeutics.—Externally preparations of thymol are used as analgesic paints and as cutaneous and general antiseptics. An alcoholic solution 1–5 per cent. may be used to disinfect the skin before operations, whilst its ointments are of value in the treatment of parasitic skin diseases. Solutions containing glycerin and oily preparations may be used in a nebuliser as disinfectants of the nasal passages.

For internal administration thymol is best prescribed in capsules; it may also be given as an emulsion. For the treatment of ankylostomiasis it is given on an empty stomach in two doses of 30 gr. at intervals of two hours, followed by a brisk purge, saline or castor oil, some six hours later. During the treatment it is important to avoid alcohol, for owing to its great solvent action on thymol there is risk of its causing the absorption of toxic quantities of the drug. Toxic effects have most commonly been produced in subjects in whom there was profound anæmia; hence it is advisable that in such subjects smaller doses should be administered.

Poisoning.—Should toxic symptoms arise the intestine should be flushed out by administering large volumes of water containing sodium or magnesium sulphate. Coffee or its alkaloids and strychnine may be required to combat the collapse, but alcohol should be avoided.[1]

P. H.

[1] Other anthelmintics are Cusso (B.P., U.S.P.), 120–240 gr. (8–16 g.), as an unstrained infusion; Cucurbitæ Seminæ Preparata (B.P.), Pepo (U.S.P.), 3–4 ozs. (80–120 g.); Embelia (B.P.), 60–240 gr. (4–16 g.), all for tape-worm; and Buleæ Seminæ (B.P.) as a powder, 10–20 gr. (6–12 dg.), for round-worm.—Ed.

CHRYSAROBIN

Chrysarobinum, Chrysarobin (B.P., U.S.P.).—Purified Araroba or Goa Powder. Araroba (B.P.) is a neutral principle, obtained from the trunk of Andira Araroba (N.O. Leguminosa), in which it is found in cavities, and is produced by a pathological process. The crude drug is boiled with benzene, the solution is evaporated to dryness, and the residue powdered.

Constituents.—The substance called chrysarobin contains four bodies, chrysarobin, methyl ether of dichrysarobin, a small amount of dichrysarobin, and another body not yet identified, but not chrysophanic acid.

Characters.—A crystalline, yellow, tasteless and inodorous powder, having an irritating effect on mucous membrane. It is soluble in hot chloroform, almost entirely soluble in hot alcohol, partially soluble in petroleum spirit, but only slightly soluble in water. With potassium hydroxide it partially dissolves and shows a deep brownish red colour. By oxidation it is converted into chrysophanic acid. "Heated with free access of air, it melts, giving off yellow fumes, and when incinerated does not leave more than 1 per cent. of ash."

Dose.—$\frac{1}{10}$ – 1 gr. (6–60 mg.), average dose $\frac{1}{2}$ gr. (3 cg.).

Administration.—It is best given in the form of a pill, made with glycerin and tragacanth. Internally, even in small doses, it gives rise to vomiting and purging; it acts as all drugs do of the anthracene group, to which it belongs. It also causes pain in the lumbar region, with voidance of urine, if acid of a yellow colour, and if alkaline reddish in appearance. The same effects are produced at times by absorption of the drug from the skin when applied as an ointment or paint.

Uses.—It is a powerful stimulant and parasiticide, and is therefore an excellent remedy in ringworm and other parasitic diseases. It is one of the best agents for treating psoriasis and has been used with good results in cases of chronic eczema, alopecia areata and other skin diseases. A suppository is said to be beneficial in hæmorrhoids.

Chrysarobin preparations readily cause erythema, and the action, therefore, needs watching; the parts of the body most susceptible are the skin of the face, scalp and genitalia. It ought not to be allowed to touch healthy skin, nor should it be applied, in any case, where there is marked hyperæmia.

Ointments of chrysarobin have the disadvantage of staining the skin, hair and linen yellow. This may be avoided by using Pigmentum Chrysarobini. Chlorinated lime will remove the discoloration.

Derivatives of chrysarobin similarly used are anthrarobin, a reduction product of alizarin (its action is slower and does not produce so much irritation; used as a 10 per cent. ointment), chrysarobin triacetate (eurobin) and chrysarobin tetra-acetate (lenirobin). Oxidised chrysarobin, being less irritating, has been recommended by Unna in the form of an ointment.

Preparations

Unguentum Chrysarobini (B.P., 4 per cent. in soft paraffin), (U.S.P., 6 per cent. in benzoated lard). Useful for psoriasis, alopecia ar-areata, or, diluted with 2 to 4 parts benzoated lard, may be applied in chronic eczema, acne and other skin affections. It is well, before using the ointment, to get rid of any old crusts of exudation.

Unguentum Chrysarobini Compositum (B.P.C.) (Unna). Chrysarobin 5, salicylic acid 2, ichthyol 3, vaseline 90.

Pigmentum Chrysarobini (B.P.C.). Chrysarobin 10 per cent. in solution of gutta-percha. To be applied with a stiff brush. In psoriasis it should be painted on twice a day, for two or three days, then washed off and further applications made.

Suppositorium Chrysarobini. Chrysarobin $1\frac{1}{4}$ gr., iodoform $\frac{3}{10}$ gr., belladonna extract $\frac{1}{7}$ gr. Glycerin *q. s.* to make a suitable paste, and cacao butter *q. s.* to 30 gr. Gives excellent results in hæmorrhoids.

Chrysarobin Sticks. Chrysarobin 30, colophony resin 5, yellow wax 35, olive oil (by weight) 30.

Chrysarobin Plaster Mulls. Contain $\frac{1}{10}$ gr. to the square inch, also made five times the strength. J. C. K.

SULPHUR AND SULPHIDES

Sulphur, a non-metallic element, is a brittle solid of a pale yellow colour. It is obtained chiefly in volcanic districts, where, as on the flanks of Etna and Hecla, it is found in large veins, from which it is quarried. It is also obtained from the native sulphides of iron and copper. It is met with in commerce as flowers of sulphur, roll sulphur, precipitated sulphur, washed sulphur and black sulphur. Two only of these are official, viz. flowers and precipitated.

Roll Sulphur—Sulphur Rotundum—is formed when the native sulphide is heated and the vapour received in a chamber kept at 120° C. where it condenses in liquid form and is then run into wooden moulds.

Washed Sulphur—Sulphur Lotum (U.S.P.) is obtained by digesting sublimed sulphur with water and ammonia, by means of which acids and arsenic are got rid of.

Average dose : 60 gr. (4 gm.).

Black Sulphur—Sulphur Nigrum (B.P.C.) *vel* Sulphur Vivum—is the residue left in the subliming pots in the preparation of sublimed sulphur —what is sold is frequently a factitious mixture of sulphur and wood charcoal.

Sulphur Præcipitatum (B.P., U.S.P.).—Precipitated Sulphur, Milk of Sulphur. It is prepared by adding hydrochloric acid to solution of calcium sulphide and thiosulphate. The sulphur is precipitated, washed and dried. The calcium preparation is obtained by boiling sulphur with calcium hydrate. If sulphuric acid be used instead of hydrochloric acid the precipitated sulphur will contain as an impurity sulphate of calcium; this used to be known as Lac Sulphuris, but it is not permissible to use it as the official article.

Characters.—A light grey or greyish yellow, smooth amorphous powder, not showing crystals of sulphate of lime, when viewed through a microscope.

Dose.—20 to 60 gr. (12–40 dg.). Average dose 60 gr. (4 gm.).

Sulphur Sublimatum (B.P., U.S.P.).—Sublimed Sulphur, Flowers of Sulphur. It is prepared by subliming the native sulphur or sulphides, the vapour being received into a large cold brick chamber.

Characters.—A bright, greenish-yellow amorphous powder possessing a faint characteristic odour. Solution of ammonia agitated with it and filtered does not on evaporation leave any residue (absence of arsenium sulphide).

Dose.—20 to 60 gr. (12–40 dg.). Average dose 60 gr. (4 gm.).

Uses.—Sulphur itself is quite inert and depends for its therapeutic action, both internally and externally, upon its conversion into sulphide.

When taken internally it passes unaltered through the stomach, but in the alkaline contents of the small intestine, a very small portion of the dose becomes sulphide and the greater part passes with the fæces unchanged. Of the alkaline sulphide formed, some is absorbed and circulates in the blood stream, being excreted by the kidneys as sulphates, by the skin and lungs as sulphuretted hydrogen; in the latter case it acts as a stimulant and expectorant. Both the breath and the skin give off the odour of sulphuretted hydrogen. The portion of sulphide remaining in the bowels slightly stimulates peristalsis, in which action the unchanged sulphur shares—possibly by mechanical irritation. The motion produced by the action of sulphur is large in amount and softer than usual, and it is unaccompanied by pain or griping. On account of its action it is useful for congestive conditions, particularly hæmorrhoids, in which it has in addition to its laxative action a soothing effect upon the vessels themselves. Its cathartic action is increased when mixed with senna, and for this purpose the confection of sulphur with confection of senna may be ordered in drachm doses at bed-time every night, or the compound liquorice powder may be taken. For children the lozenge may be ordered, which contains in addition to sulphur, the acid tartrate of potassium. It is used also as a liver stimulant where the secretion of bile is diminished. For chronic rheumatism it finds favour with some, in the form of compound confection of guaiacum, although it is probable that the guaiacum has more effect than the sulphur.

Sulphur has been found useful in preventing fermentation in cancer of the stomach. On account of its stimulating action on the respiratory passages it is used in chronic bronchitis. In the form of powder blown on the fauces it has an excellent effect in septic conditions of the throat, the sulphur readily becomes changed to sulphuretted hydrogen by the faucial secretions, and then exerts its effect on germs of disease.

Sulphur waters have a similar action to the sulphur itself; they are tonic and stimulating, whilst in syphilis they facilitate the absorption of large doses of mercury, and assist a patient non-tolerant of mercury to take the drug. They minimise the poisonous effect of mercury in these cases without interfering with their specific action.

Externally, sulphur, in the form of ointment alone or combined with other drugs such as resorcin, acts as an antiseptic and parasiticide in such cases as seborrhœa, acne, chronic eczema and scabies; in the latter the ointment made with sublimed sulphur is to be preferred to one containing the precipitated drug, since the particles of sulphur in the former being more gritty they act mechanically in opening up the burrows of the insect.

Vleminckx's Solution—Sulphurated Solution of Lime—acts more effectively than the ointment. Sulphur in the form of emulsion is excellent for swabbing out cavities in dentistry, and is useful for "cleaning up" septic or tuberculous wounds.

In the form of baths, made with natural water, or prepared from the sulphides, it has an excellent effect in rheumatism, gout and skin diseases.

For fumigating rooms, after infectious disease, sulphur is burnt either as a candle with a wick running through it, or by burning it on glowing coals. The proportion to use is one pound to 1,200 cubic feet of space.

What has been stated above applies to both the sublimed and the precipitated varieties of sulphur; it is found, however, that when the precipitated variety is taken, the kidneys excrete four or five times as much, in the form of sulphate, as when sublimed sulphur

is administered, showing the more ready conversion of the former into alkaline sulphide.

Uses of the Sulphides.—These combinations of sulphur taken internally have the same effect, though in a more marked degree, as if sulphur itself be taken. The potash salt used to be given frequently, but its place is now taken by that of calcium.

Externally they possess all the properties of sulphur, but the preparations, breaking up more readily, are more likely to set up irritation.

Sulphurated lime is used internally to arrest and prevent suppuration, as in boils, carbuncles and acne, whilst externally applied it acts as a depilatory.

Sulphurated Potash, as the ointment is serviceable in treating eczema, acne, etc. It also is the usual salt employed for making sulphur baths, which are useful in gout, rheumatism, joint affections and chronic skin diseases; for scabies a stronger bath is necessary.

Sulphurated Antimony in gout and rheumatism is useful as a cholagogue, especially in combination with other drugs, *e. g.* Pilula Hydrargyri Subchloridi Composita. Occasionally it is prescribed as a diaphoretic.

Preparations of Precipitated Sulphur

Colloidal Sulphur. Prepared by precipitating sulphur from a mixture of sulphides and polysulphides with an acid in the presence of albumin. It is used in a spray as an emulsion, for acne, and is said to be better than the official variety.

Confectio Sulphuris (B.P.). Precipitated sulphur 45, acid potassium tartrate 11, tragacanth 0·5, syrup 21, tincture of orange 5·5, glycerin 17.
Dose: 60–120 gr. (4–8 g.).

Jephson's Powder. Precipitated sulphur 2, guaiacum resin 1.
Dose: 60 gr. (1 g.) Used for tonsillitis of rheumatic origin, acne and constipation.

Lotio Plumbi et Sulphuris (B.P.C.). Sulphur hair restorer. Acetate of lead 1·75, precipitated sulphur 3·5, spirit of rosemary 2·5, glycerin 12·5, distilled water *q. s.* to produce 100. This lotion represents the commercial "Hair Restorer." It causes the hair to become of a dark brown colour owing to formation of lead sulphide in the hair shaft. It may be improved by making it up with rosewater, or adding a perfume to it.

Lotio Sulphuris (B.P.C.). Sulphur Lotion. Precipitated sulphur 6·65, glycerin 3·12, alcohol 12·5, rosewater 40, lime water to produce 100. An elegant lotion for acne.

Pastillus Sulphuris Compositus (B.P.C.). Compound Sulphur Pastille. Precipitated sulphur 5gr., acid potassium tartrate 1gr., a sufficiency of glyco-gelatin basis to make one pastille.

Pulvis Guaiaci Compositus. Compound Guaiacum Powder—"Chelsea Pensioner." Precipitated sulphur, guaiacum resin, heavy magnesium carbonate, gum acacia and bicarbonate of potash, equal parts of each.
Dose: 20–40 gr. (12–24 dg.).

Trochiscus Sulphuris. Sulphur Lozenge (B.P.). Precipitated sulphur 5 gr., acid potassium tartrate 1 gr., a sufficiency of a basis made with sugar, gum acacia, mucilage of acacia and tincture of orange to make one lozenge. Lozenges are an excellent method of administering sulphur. They are readily taken by children.
Dose: 1–6 lozenges.

Unguentum Sulphuris et Acidi Salicylici. Sulphur and Salicylic Acid Ointment. Precipitated sulphur 30 gr., salicylic acid 30 gr., vaseline 1 oz. For Alopecia Furfuracea—Apply at night and well wash with soft soap and water following day.

Preparations of Sublimed Sulphur

Confectio Guaiaci Composita. Compound Guaiacum Confection—"Chelsea Pensioner." Guaiacum 2, sublimed sulphur 13, magnesium carbonate 2, ginger 1, treacle, by weight, 12.
Dose: 1–2 dr. Used as a laxative for rheumatic patients.

Confectio Senna et Sulphuris. Confection of senna, confection of sulphur, equal parts of each.
Dose: 60–120 gr. (4–8 g.). Useful in hæmorrhoidal conditions.

Emulsio Sulphuris. Sublimed sulphur 120 gr., almond or olive oil 4 oz. Useful for swabbing out septic or tuberculous wounds and cavities.

Parogenum Sulphuris (B.P.C.). Sulphur Parogen—Sulphur Vasoliment. Sublimed sulphur 3, linseed oil 37, parogen *q. s.* to produce 100. Used in place of sulphur ointment in parasitic diseases.

Parogenum Sulphuris Compositum (B.P.C.). Compound Sulphur Parogen—Compound Sulphur Vasoliment. Sulphur parogen 10, oil of cade 10, thymol 0·3, eucalyptol 3, oil of turpentine 30, parogen *q. s.* to produce 100. It is antiseptic and parasiticide. Useful in chronic skin diseases.

Pulvis Glycyrrhizæ Compositus (B.P.). Compound Liquorice Powder. Senna 2, liquorice root 2, fennel fruit 1, sublimed sulphur 1, sugar 6·5.
Dose: 60–120 gr. (4–8 g.). It is a mild laxative and useful in constipation and congestive conditions. Being pleasant, children take it readily.

Pulvis Glycyrrhizæ Compositus (U.S.P.). Senna 18, liquorice root 23·6, washed sulphur 8, oil of fennel 0·4, refined sugar 50.
Dose: 60 gr. (4 g.).

Unguentum Sulphuris (B.P., 10 per cent. in benzoated lard.) (U.S.P., 15 per cent. of Sulphur Lotum in benzoated lard.) Useful in scabies and acne, after the part has been well washed with soft soap and water. The ointment made with sublimed sulphur is preferable to one made with precipitated sulphur (*vide Sulphur-Uses*).

Unguentum Sulphuris Compositum. Compound Sulphur Ointment—Unguentum ad Scabiem Viennense. Wilkinson's Ointment. Sublimed sulphur 15, precipitated chalk 10, tar 15, lard 30, soft soap 30. A good remedy for scabies and psoriasis.

Unguentum Sulphuris Camphoratum (B.P.C.). Camphorated Sulphur Ointment. Sublimed sulphur 2, carbolic acid 3, resorcin 3, camphor 3, solution of coal tar 5, benzoated lard 42, white soft paraffin *q. s.* to produce 100.

Unguentum Sulphuris et Resorcini (B.P.C.). Sulphur and Resorcin Ointment. Sublimed sulphur 4·5, resorcin 3, yellow soft paraffin *q. s.* to produce 100. Both these ointments are beneficial in acne, eczema and chronic skin diseases.

Unguentum Sulphuris Hypochloritis. Sulphur Hypochlorite Ointment. Sublimed sulphur 12, sulphur chloride 2, essential oil of almonds by weight 2, lard 84. Used for psoriasis, scabies, etc. For sensitive skins use an ointment half this strength.

Unguentum Sulphuris Iodide (B.P., 1898.). Iodide of sulphur 20, glycerin 20, benzoated lard 460. The action of the iodide of sulphur is that of iodine rather than sulphur. It is used in acne, scabies and other parasitic affections of the skin.

Antimonium Sulphuratum (B.P.). Sulphurated Antimony. A mixture containing antimony sulphides and oxides.

Dose: 1–2 gr. (6–12 cg.). Contained in Pilula Hydrargyri Subchloridi Composita.

Antimonii Sulphidum. Purified Black Antimony (B.P., 1898). It is prepared by purifying native antimony sulphide, and is used to prepare the sulphurated salt.

Carbonis Disulphidum (B.P.). Carbon Disulphide. Syn. Alcohol Sulphuris—Carbonei Disulphidum (U.S.P.). It is made by passing the vapour of sulphur over red-hot carbon and purifying. It is used for dissolving phosphorus and indiarubber, though the vapour is sometimes applied locally to the skin for neuralgia and enlarged glands. For this purpose cotton-wool, saturated with the liquid, is placed in a wide-mouthed bottle, and the mouth of the bottle placed in contact with the part for a few minutes at a time.

Calx Sulphurata (B.P., U.S.P.). Sulphurated Lime. Syn. Calcii Sulphidum. It is prepared by reducing native sulphate of lime with carbon.

Dose: ¼ to 1 gr. (16–60 mg.). It is best given in the form of a pill made with glucose, making the total weight of the pill up to ½ or 1 gr. with sugar of milk. The pills should be varnished.

Preparation.—Liquor Calcis Sulphuratæ (B.P.C.). Solution of Sulphurated Lime. Syn. Lotio Calcis Sulphurata; Solutio Sulfureti Calcici; Vlemenckx's Solution. Quicklime 2, sublimed sulphur 5, water *q. s.* to 100. Diluted with one or more parts of water, this solution is used as a paint for scabies. For a bath, in chronic psoriasis or other skin diseases, use a dessertspoonful to each gallon of water. The solution should be prepared in a well-enamelled or porcelain dish.

Sulphurated Lime Depilatory. To make this Milk of Lime is charged with sulphuretted hydrogen.

Potassa Sulphurata (B.P.). Sulphurated Potash, Liver of Sulphur, Hepar Sulphuris. Prepared by heating potassium carbonate and sulphur in a crucible until effervescence has ceased and the whole is in a state of perfect fusion. It is then poured out and allowed to solidify.

Characters.—In solid greenish fragments, which are liver brown when recently broken. Its aqueous solution has the odour of sulphuretted hydrogen, and evolves it freely when hydrochloric acid is added.

Dose: No dose is official, but it may be given in quantities of 1 to 5 gr. in pill or solution.

Preparations.—Unguentum Potassæ Sulphuratæ. Sulphurated potash 30 gr., hard paraffin ¼ oz., soft paraffin ¾ oz. It is useful for ringworm, but should be recently prepared.

Balneum Sulphuratum (B.P.C.). Sulphurated Potash 4 to 7½ oz. Water, 30 gall. The Barègés waters are more agreeable and may be made with sodium sulphide, sodium carbonate, sodium chloride, 20 gr. of each to the gallon. A convenient form is Bain Sulfuré Liquide. Sulphurated Potash 1, water 2. Dissolve, filter and preserve in stoppered bottle. To be added to water as required.

Sodii Sulphidum. Description—Yellowish deliquescent crystals soluble in water. Used in skin affections and in 25 to 40 per cent. aqueous solutions as a depilatory.

Preparation.—Balneum Sulphuris Alkalinum. Sulphide of sodium 2 oz., chloride of sodium 2 oz., bicarbonate of sodium 1 oz. Add to 50–60 gallons hot water.

J. C. K.

BORIC ACID AND BORAX

Boric acid, H_3BO_3, and borax, $Na_2B_4O_7$, are very extensively used in medicine, more commonly externally than internally. Boric acid is a weak acid and when dissolved in water its salts undergo hydrolysis, yielding alkaline solutions. The acid is soluble to the extent of 4 per cent. in water at ordinary temperatures. Solutions of the acid have a very slight antiseptic action in that they retard the growth of bacteria without killing them; they are effective in preventing the growth of many moulds. It is necessary for the solutions to be nearly saturated for their antiseptic action to be of practical value.

Externally, boric acid is used as a mild antiseptic; mixed with starch, talc or zinc oxide it is used as a dusting powder, and ointments containing boric acid are also employed. When applied continuously for long periods irritation of the skin is not uncommon, and from raw surfaces sufficient may be absorbed to give rise to toxic symptoms.

Borax is slightly alkaline, and like boric acid is much used as a preservative and in the preparation of lotions, injections and gargles.

When taken internally boric acid is but slightly toxic, though large quantities cause gastro-intestinal irritation, vomiting and purging. Its absorption is fairly rapid, so that it is of little utility as an intestinal antiseptic. The evidence as to the action of small quantities of borates when taken for prolonged periods is somewhat conflicting, though it is a matter of considerable importance in view of the extensive employment of boric acid and borax as preservatives of foods. Healthy adults appear to be affected but little, but children and young animals are more susceptible. There is evidence that the absorption of foodstuffs, particularly fats and proteins, may be considerably delayed with consequent failure of nutrition. Some investigators hold that there is an increased breakdown of the fats of the tissues. In consequence of the accumulation of evidence of the unfavourable action of borates their employment as preservatives of milk, cream and other foods is now regulated in many countries, and usually they are not allowed to exceed 0·5 per cent.

Apart from gastric and intestinal symptoms, affections of the skin such as papular eruptions and localised œdema and albuminuria have been observed. Nervous phenomena such as sleeplessness, muscular weakness and headache and even collapse and death have also been described. In some cases poisonous symptoms have arisen owing to solutions used for irrigating cavities having been left *in situ*.

The excretion of boric acid and borax in the urine begins very shortly after the administration of the drug; the greater portion is excreted within twelve hours, but the remainder much more slowly, and traces may be detected in the urine for several days. In consequence of this delayed excretion borates and foods preserved with them should be avoided by patients suffering from renal disease with defective excretion.

Borax is incompatible with mineral acids and their salts, with heavy metals and with mucilage of gum acacia. In solution it precipitates many alkaloids.

Acidum Boricum (B.P., U.S.P.).

Dose: 5–15 gr. (3–10 dg.).

Pulvis Acidi Borici et Amyli (B.P.C.). Equal parts of boric acid and starch.

Pulvis Talci Boricus (B.P.C.). 1 part in 10.

These two are used as antiseptic dusting powders.

Carbasus Acidi Borici (B.P.C.). Boric acid gauze.

Gossypium Acidi Borici (B.P.C.). Boric acid wool.

Linteum Acidi Borici (B.P.C.). Boric acid lint.

These three each contain 40 per cent. boric acid and are used as antiseptic dressings. They should be kept in sealed packets until required for use.

Lotio Acidi Borici (B.P.C.). 1 in 30. Used as a mild antiseptic lotion and for fomentations.

Balneum Acidi Borici (B.P.C.). 1 in 80. Used in irritable skin diseases.

Collyrium Acidi Borici (B.P.C.). A 2 per cent. solution which should be diluted with an equal quantity of warm water before use as an eye lotion.

Collyrium Acidi Borici et Zinci (B.P.C.). 1 per cent. of boric acid and 0·1 per cent. zinc sulphate in rose water; it is used when an astringent eye lotion is required.

Boroglycerinum (B.P.C.). Contains approximately 50 per cent. boric acid.

Glycerinum Acidi Borici (B.P.). Contains 30 per cent. boric acid.

Glyceritum Boroglycerini (U.S.P.). Contains 30 per cent. boric acid.

These three preparations are much used in the preparation of antiseptic fomentations and in the treatment of ulceration of the mouth in children.

Mel Boricum (B.P.C.). 1 in 10. The glycerinum is preferable.

Pastillus Acidi Borici (B.P.C.). 2 gr. in each.

Pessus Acidi Borici (B.P.C.). For vaginal use, 10 gr. in each.

Solvellæ Acidi Borici (B.P.C.). 15 gr. Used for the preparation of solutions.

Solvellæ Antisepticæ (B.P.C.). Contain boric, benzoic and carbolic acids together with thymol and essential oils. Dissolved in a wineglass of water they yield a pleasant antiseptic mouthwash.

Tinctura Antiseptica (B.P.C.). Contains boric and benzoic acids, thymol, eucalyptol and other essential oils. A small quantity added to water forms an antiseptic mouthwash.

Oculentum Acidi Borici (B.P.C.). 4 per cent. ointment in soft paraffin for ophthalmic purposes.

Unguentum Acidi Borici (B.P.). 10 per cent. in paraffin ointment.

Unguentum Acidi Borici (U.S.P.). 10 per cent. similar to the above.

Borax Purificatus (B.P.). **Sodii Borax** (U.S.P.).
Dose : 5–15 gr. (3–10 dg.).

Gargarisma Boracis (B.P.C.). 4 per cent. Used in stomatitis.

Collyrium Boracis (B.P.C.). 2 per cent.

Lotio Boracis (B.P.C.). 2 per cent. in rose water.

Liquor Boracis Compositus (B.P.C.). Dobell's solution. Contains 1·5 per cent. borax together with sodium bicarbonate and phenol; it is widely used for nasal irrigation.

Glycerinum Boracis (B.P.). 1 in 6.

Mel Boracis (B.P.). Borax 1, glycerin 5, honey 85.

These two preparations are acid in reaction and effervesce with carbonates. They are much used in the treatment of stomatitis in children. The glycerinum is preferable since the residue of the honey preparation is liable to undergo bacterial fermentation in the mouth when diluted by the saliva.

Pastillus Boracis (B.P.C.). 3 gr. in each.

Trochiscus Boracis (B.P.C.). 3 gr. in each. Used in stomatitis.

Solvellæ Boracis Compositæ (B.P.C.). One dissolved in 2 oz. water makes a solution suitable for nasal irrigation.

Solvellæ Boracis et Cocainæ Compositæ (B.P.C.). Contain borax, boric and benzoic acid, essential oils and cocaine hydrochloride. One dissolved in 2–3 oz. water makes a solution for nasal irrigation.

Solvellæ Borosalinæ (B.P.C.). Contain 5 gr. each of borax and salt.

Solvellæ Borosalinæ Fortes (B.P.C.). Contain 10 gr. each of borax and salt.

These two are used in the preparation of mildly antiseptic salt solutions.

Unguentum Boracis (B.P.C.). 1 of borax in 8. It is more soothing than the boric acid ointment and more suitable for application to the broken skin of chilblains, chapped hands and cracked nipples.

Boric acid and borax are used externally as mild antiseptics in the dressing of wounds and as lotions for irrigating the eye, ear, nose, stomach, bladder and septic cavities. The solutions are of value chiefly on account of their non-irritant character, though it is doubtful if their efficacy much exceeds that of sterile normal saline. Over the latter they have the advantage that they do not become reinfected if exposed to the air, though it is important that the solution should not be permitted to remain in the cavity irrigated, for serious symptoms have arisen owing to the absorption of the boric acid contained.

Internally, borax was formerly used in the treatment of epilepsy and as a solvent of uric acid calculi, but its efficacy has not been demonstrated. In the treatment of infections of the urinary tract boric acid given by the mouth has shown itself to be of great value, for it renders the urine acid and when administered in conjunction with urotropin sets free formaldehyde, which is then able to exert its specific action on the infecting organisms. The concentration of the boric acid in the urine is not sufficient of itself to exert any appreciable action. J. C. K.

HYDROGEN PEROXIDE

Preparation.—Liquor Hydrogenii Peroxidi (B.P.). Aqua Hydrogenii Peroxidi (U.S.P.). Solution of Peroxide of Hydrogen. This is a solution of hydrogen peroxide made by the action of a dilute mineral acid, preferably sulphuric, on peroxide of barium, in the presence of water at a temperature below 10° C.

Characters.—A colourless and inodorous liquid, with a slightly acid taste, producing in the mouth a peculiar sensation and soapy froth. It should contain about 3 per cent. of hydrogen peroxide, corresponding to 9 to 11 volumes of oxygen.

Dose : ½ to 2 fl. dr. (2–8 ml.). Average dose, 1 dr. (4 ml.). It is liable to deterioration by keeping, and a small amount of phosphoric acid may be added to it as a preservative.

Uses.—It owes its action to the liberation of oxygen, and for this reason it has been

given in diabetes, uræmia, epilepsy, pertussis, pneumonia and phthisis, but with doubtful benefit.

Its use externally is most beneficial in all septic conditions, discharging ulcers, abscesses, venereal sores, and for washing out cavities such as in connection with the teeth or empyema; care, however, must be taken that there is free passage for the back flow, or, owing to the liberation of oxygen, air emboli may be formed and cause death. It has also been used locally for inoperable cancer of the womb, chilblains and lupus favus.

It relieves the pain from stings of insects immediately.

For skin diseases a useful ointment may be made with anhydrous wool fat and 2 per cent. of the solution.

An injection into the nose acts immediately in controlling *epistaxis*. It bleaches hair and is sold commercially as "Golden Hair Dye."

For diphtheria and scarlatinal otitis a spray of one part of the solution to seven parts of water will be found useful, and in the latter after washing out the canal with boric acid solution, a little of the solution may be instilled. This is followed by a bubbling of the oxygen, and helps considerably to clear up the disease.

Merck states that pain and burning sensation in the stomach after a dose of perhydrol (a stronger solution than the above) is diagnostic of ulceration of the stomach.

Preparations

Ozonic Ether or Pyrozone. It is a solution of 1 to 2 per cent. of hydrogen peroxide in ether. With Tincture of Guaiacum it forms a test for blood.

Dose: ½–1 fl. dr. (2–4 ml.).

Gargarisma Hydrogenii Peroxidi. Peroxide of hydrogen solution 1 dr., chloride of sodium 5 gr., glycerine 30 min., water to 1 fl. dr. For septic tonsillitis, etc.

Hydrogenii Peroxidum Boratum. Borated Peroxide of Hydrogen. It is made by neutralising peroxide of hydrogen with caustic soda, and adding, in the cold, 3 per cent. of boric acid. Makes a useful mouth-wash for dental work or gargle for pharyngeal affections.

Magnesii Peroxidum (B.P.C.). Peroxide of Magnesium. A white tasteless powder, insoluble in water.

Dose: 30–60 gr. (2–4 g.). Given for weak digestion, anæmia, diarrhœa of phthisis, anorexia, flatulence and pyrosis. It is contained in "Hopogan" and "Magnesium Perhydrol."

Sodii Peroxidum (B.P.C.). Peroxide of Sodium. A yellowish white, amorphous, deliquescent powder. Dissolves in water with production of heat and evolution of oxygen. Unna recommends a soap containing 10 to 20 per cent. of it, in acne.

Zinci Peroxidum (B.P.C.). Peroxide of Zinc. A white powder insoluble in water. Used locally in skin diseases. It helps the healing of chronic ulcers. It is known also as "Ektogan" and "Dermogen."

Zinci Perhydrol. This is similar to Zinci Peroxidum and is used in the form of ointment—20 gr. to an ounce of soft paraffin—for skin diseases.

Cubes of Sodium Peroxide are sold for placing in a patent oxygenator to purify the air of rooms.

Menthoxal is a 3 per cent. solution of hydrogen peroxide with menthol.

Camphoroxal and Naphthoxol are similar solutions, but camphor and naphthol take the place of the menthol.

The basis of the popular disinfectant Sanitas is hydrogen peroxide. J. C. K.

OXYGEN

The inspired air contains approximately 21 per cent. of oxygen, 79 per cent. of nitrogen, 0·03 per cent. of carbon dioxide and a variable amount of water vapour. The expired air is saturated with water vapour and contains about 3·5–4 per cent. of carbon dioxide, 16·5–17 per cent. of oxygen and 79·5 of nitrogen. The pulmonary alveolar air is saturated with water vapour and contains about 13–14 per cent. of oxygen and 5–6 per cent. of carbon dioxide.

As the pressure of the water vapour in the alveolar air which is saturated at body temperature equals 49 mm. Hg., the pressure of oxygen in the pulmonary alveoli at sea level may be taken as equal or $\frac{(760 - 49) \times 14}{100}$, or approximately 100 mm. Hg., and the pressure of carbon dioxide is equal to $\frac{(760 - 49) \times 5{\cdot}6}{100}$, or approximately 40 mm. Hg. The breathing is regulated by the concentration of acid in the blood, which circulates through the respiratory centre; the centre responds to the stimulus so as to keep the concentration of acid in the blood constant. Dyspnœa is provoked during muscular exertion by the increase of acid in the blood. The acid may be carbonic acid or other acids, such as lactic, which are produced in the tissues when there is a deficiency of oxygen. After a period of severe exertion lactic acid can be detected both in the blood, sweat and urine.

The effects which result from a deficiency of oxygen are the same whether the percentage or the pressure of oxygen in the atmosphere is diminished. This is proved by laboratory experiments, by experience in high altitudes, and of the air in mines. In the combustion of fuel it is the percentage of oxygen in the air that matters, but in the respiration of man it is the weight in a given volume that counts. A cubic foot of air, with an oxygen percentage of 17·5 at sea level, contains about the same weight of oxygen as a cubic foot of air at an altitude of 5000 feet with an oxygen percentage of 21. A lamp will scarcely burn in the former atmosphere, but quite readily in the latter; for respiration they are alike available. The barometer may vary at sea level between 28 and 31 inches; between these levels the partial pressure of oxygen is reduced about 10 per cent. That is to say, when the barometer falls to 28 inches the pressure of oxygen corresponds to 18 per cent. of an atmosphere measured at 31 inches, in place of 21 per cent. The atmospheric pressure is diminished 25 per cent. or even more at the famous Alpine mountain health resorts. This produces no discomfort in a newcomer, except perhaps slight breathlessness on exertion.

The experimental diminution of oxygen percentage from 21 per cent. to 15 per cent. at sea level is practically without effect on man. The ill-effects, then, which are felt in crowded confined atmospheres cannot be attributed to the diminution of the oxygen percentage. Neither can they be ascribed to the increase in the percentage of carbonic acid, for the partial pressure of CO_2 in the lungs is kept constant by the action of the respiratory centre, this in its turn being regulated by the concentration of acid in the blood, which circulates through it. Thus the slight increase in percentage of carbonic acid which occurs in crowded rooms has no other effect than that of increasing slightly the pulmonary ventilation, in just such measure as to keep the partial pressure of CO_2 in the lungs constant. The bad effects of the crowded room and the good effects of open-air treatment alike depend on the physical qualities of the air; its coolness, movement and relative dryness, which powerfully influence the skin and respiratory mucous membrane, stimulate the nerve-endings, govern the rate of heat loss and metabolism of the body.

When the percentage of oxygen at sea level is lowered below 15, symptoms first appear, muscular exertion becomes less easy, and there is slight dizziness and an unusual shortness of breath. A person not exerting himself will generally notice no change until the oxygen percentage has fallen even to 10–12 per cent. The breathing then becomes deeper and more frequent, the pulse accelerated and the face takes on a dusky tint. At about 7 per cent. the mind becomes confused and the senses dulled, muscular power greatly impaired; there is usually distinct panting, the heart palpitates, and the face is leaden in colour. At a slightly lower percentage consciousness is lost. At high altitudes the same symptoms occur at partial pressures which are equivalent to those at sea level, thus life is in imminent danger when the pressure sinks to about one-third of an atmosphere, corresponding to a height of about 30,000 feet. Such altitudes can only be reached in safety if the subject wears a breathing apparatus and inhales oxygen. Since the discomfort produced by want of oxygen is very slight, the subject receives little indication of danger, and it is thus most foolhardy to venture into places where oxygen is deficient, *e.g.* foul sewers and wells, and mine-workings full of fire-damp. In the total absence of oxygen consciousness will be lost in about 30 seconds and without warning. Carbon monoxide, which is present in after-damp of mines and in house gas, robs the body of oxygen by combining with hæmoglobin. It has so great an affinity that when 0·08 per cent. is present in the air and this is breathed long enough, about half the hæmoglobin will become saturated with CO. An apparatus for breathing oxygen must be used for investigating all places where a deficiency of oxygen or presence of CO is suspected. The atmosphere can be tested by the introduction of a small bird, which, owing to the great rate of its metabolism, will become ill in a much shorter time than does a man.

The rate of metabolism of the body, controlled as it is by the nervous system, is not altered by the breathing of oxygen. The body cannot be forced to burn more quickly like a fire. The breathing of oxygen has no effect on the normal resting man other than a slight slowing of the pulse, but it enables a man to hold his breath longer, and to carry out strenuous exertion more easily. This is because the breathing and the action of the heart are closely dependent on the concentration of acid in the blood. The acid in the blood may be carbonic acid, or other acid, such as lactic, which appears in the blood whenever there occurs a want of oxygen in the tissues. The normal resting man does not lack oxygen, and only a trace of lactic acid can be detected in his blood. On the other hand, after a period of exertion accompanied by dyspnœa, lactic acid, as already mentioned, can be detected both in his blood and urine. The presence of other acids in the blood excites dyspnœa, for they add their effect to that of the carbonic acid, the respiratory centre responding to the total acidity of the blood.

By breathing oxygen during the exertion the

lack of oxygen in the muscles is lessened, the production of lactic and similar acids diminished, and hence the breathlessness is less, and the capacity and ease of working greater.

The condition of second wind probably depends on the adjustment of the concentration of acid in the blood, CO_2 is washed out by hyperpnœa so as to compensate for the production of lactic acid. An athlete who breathes deeply and inhales oxygen immediately before a race washes CO_2 out of his body, thoroughly oxygenates his blood, and starts the race with his lungs full of oxygen. He is thus able to run in a shorter time and more easily a quarter mile, and has less stiffness of his muscles after the race. If he breathes oxygen, immediately after the race he will be fit sooner to run again, for the acid substances are removed by the oxygen—probably built up again into muscle substance. The frequency of the pulse is diminished by breathing oxygen, both before and after a piece of violent exertion.

After deep breathing for two or three minutes, and filling the lungs with oxygen, it is possible to hold the breath without any effort for four or five minutes; the desire to breathe does not become irresistible until the acid in the blood rises above the normal concentration.

It is possible to breathe oxygen containing a concentration of CO_2 which cannot be endured in the presence of air. This is because the oxygen checks the formation of other acids in the blood which would otherwise add their effect to that of the carbonic acid.

By inhaling 3 per cent. of CO_2 the pulmonary ventilation is increased about 100 per cent. and this increase is not noticed by a man at rest.

The simplest way to make a patient breathe deeply is to let him breathe in and out through a length of hose-pipe ($\frac{3}{4}$–1 inch internal diameter) say two feet long. He then inhales some of his own exhaled air, and the CO_2 in this increases the pulmonary ventilation. This is the best method of causing expansion of the lung after the chest has been opened by the surgeon for relief of empyema, the diminution of oxygen brought about by inhaling air through the pipe will not matter. If it is desirable to give the patient oxygen also, the gas can be allowed to escape from a cylinder through a side tube into the pipe a couple of feet from the mouth, the pipe then being made a foot or two longer.

In the attenuated atmosphere of high altitudes the hyperpnœa of the newcomer is provoked by the deficiency of oxygen and the conseqnent increased acidity of the blood. A readjustment of the acid and bases in the blood is then brought about by the secretory activity of the kidneys; as the relative proportion of other acids is increased that of carbonic acid is lowered. It is washed out of the body by the hyperpnœa until the concentration of acid in the blood is brought to about the normal. On the top of Pike's Peak the pressure of carbonic acid in the alveolar air was found to be thus lowered, *e.g.* from 40 to 27 mm. Hg. (barometer = 459 mm. Hg.), and as a result of this the pressure of oxygen in the alveolar air was raised from $38\frac{1}{2}$ to $53\frac{1}{2}$ mm. Hg., an adjustment which made life possible, for the hæmoglobin took up more oxygen in the lungs, both because the pressure of oxygen there was raised and that of carbonic acid lowered. The acid produced in the tissues aids in the dissociation of the oxyhæmoglobin there. On reaching high altitudes the blood concentrates owing to the passage of water into the tissues, more red corpuscles are formed by the activity of the red marrow, the total volume of hæmoglobin is increased, and thus the better carriage of oxygen secured. The attenuated air of high altitudes thus acts as a valuable method of treatment, stimulating a better ventilation of the lungs, altering the acid value of the blood and provoking the formation of blood. At the same time the cool moving air and sunlight affect the skin, stimulate the metabolism, and increase the vigour of the body. The readjustment of the acid and base in the blood on returning from high altitudes to the plains is not completed under about 14 days. At the end of this time the alveolar pressure of CO_2 is restored to the normal value at sea level.

After acclimitisation at high altitudes the subject can do hard work up to a certain degree without undue breathlessness, but this degree is lower than at sea level. The excess of acid is more easily produced in him owing to the attenuation of the air.

The symptoms of mountain sickness, dizziness, headache, faintness, sickness, shortness of breath, inability to make any effort and blueness of the face, are immediately removed by the inhalation of oxygen, only to return again when the oxygen is removed. The aeroplanist or balloonist can safely reach record altitudes only by wearing an oxygen-breathing apparatus, and starting to breathe oxygen before reaching a dangerous altitude. The writer has contrived a portable apparatus which allows the generation and breathing of oxygen at high altitudes, and it has been used with advantage by some who have had to visit the lofty parts of Mexico and the slopes of the Himalayas, in particular by one, the subject of a weak heart. This apparatus consists of a vulcanised pure rubber bag with a metal box at one end and a mouthpiece controlled by a clip at the other end. Into the box are placed two cakes of oxylithe (peroxide of sodium), the bag is emptied of air, and into it, through the mouthpiece, is introduced a pint of water, the box being held above the

level of the bag. The clip is then closed, and the bag raised so that the water enters into the box. Oxygen is generated and fills the bag, and a solution of caustic soda is left. The nose is then pinched or clipped, and the mouth applied to the mouthpiece, and the clip on this opened. The subject breathes in and out of the bag, and shakes the caustic soda solution gently so as to absorb the exhaled CO_2. Two cakes give him enough oxygen to breathe for 20 minutes or more. The cakes are packed in flat air-tight tins, and the apparatus folds into a small compass. This apparatus is one which is of use in hinterlands where cylinder oxygen cannot be obtained.

Oxygen is the one treatment of value for those who are "gassed," *i.e.* poisoned with carbon monoxide. A mouse which has become moribund after inhalation of coal gas immediately recovers on being placed in a chamber full of oxygen and compressed to two atmospheres. Enough oxygen is then *dissolved* in the plasma to compensate for the lack of oxygen brought about by the union of hæmoglobin with carbon monoxide. As pressure chambers are not available, the next best thing is to force oxygen into the patient's lungs. This can be effected by means of a rigid tube inserted in one nostril and connected to an oxygen cylinder by a length of *pressure* tubing. The cylinder valve is opened wide enough to give a fairly forcible current, and the mouth of the patient held closed. The oxygen is made to blow up the lungs by pinching the nostrils, on letting go the nose the oxygen escapes. The operation is performed fifteen times a minute and thus artificial respiration is effected. In an emergency, where tubes are lacking the nozzle of the cylinder could be inserted into the nostril *after turning on the current*. Mr. R. H. Davis and the writer have invented an artificial breathing apparatus [1] to be used with oxygen for the resuscitation of those "gassed," apparently drowned, etc. The face mask is fitted with a pneumatic rubber collar and is strapped to the face; before strapping up the mask the tongue is pulled out by means of tongue-forceps which are inserted through the front of the mask by means of a flexible air-tight attachment. Two tubes, wide in bore, open into the mask. The bellows are rhythmically operated by means of the handle. Each downstroke forces oxygen into the lungs through tube A, each upstroke fills the bellows with oxygen from the bag C, and at the same time operates a valve, placed at the end of the tube B, so that the gas in the lungs escapes. Thus expiration is brought about by the natural recoil of the thorax. The bag C is filled with oxygen from the cylinder through a reducing valve, and the bellows are worked at such rate that the oxygen supply keeps pace with the delivery. The operator, watching the bag C, regulates the frequency of his strokes so as not to empty it. The reducing valve is arranged to give seven litres a minute. It is inadvisable to use apparatus which exert an expiratory suction on the lungs. True, such forms of apparatus have been placed on the market and widely advertised, viz. the Pulmeter and Lungmeter. It has been shown by an American committee of physiologists that the suction force collapses the larger bronchial tubes, does not bring about an efficient expiration, and is therefore dangerous.

To administer oxygen efficiently to cases of pneumonia, the writer has contrived a light form of mask.[2] It consists of a concave piece of celluloid, round the margin of which a light curtain of washable material is hung. A handle which serves also as the oxygen tube is attached, and a support which allows the mask to rest comfortably on the body of the patient, while the operator attends to the cylinder, etc. When the mask is in position the curtain drops down upon the margin of the face and the patient breathes the atmosphere beneath the mask. The cylinder valve must be opened wide enough to give a pleasant cool current and drive the exhaled CO_2 out of the mask. The operator can find out the right force of the current upon himself, and having once determined what is comfortable, can at any time turn on the cylinder so as to give a similar strength of current when momentarily tested upon his lips. By this means the patient gets 60 to 70 per cent. of oxygen in his alveolar air. By the ordinary method of giving oxygen through a tube or funnel held near the nose, the oxygen percentage in the lungs is not raised more than 1–2 per cent. above the normal, for nearly all the oxygen escapes into the atmosphere and is wasted. To open a cylinder of oxygen in a room, and expect the percentage of the atmosphere therein to be raised is as absurd as to make water into the sea and expect the percentage of salt to be increased. In using the writer's mask there is no need to warm the oxygen or moisten it by passing it over water. It has been suggested that alcohol vapour may be added to the oxygen with advantage. The writer has contrived a metal box for effecting this purpose. An ordinary electric lamp is placed at the bottom of the box, and a pot containing whiskey or brandy above it. The oxygen current passes through the box and takes up the alcohol evaporated by the heat of the lamp. On giving oxygen efficiently with this mask the writer has observed the failing pulse of patients dying from

[1] Made by Messrs. Siebe Gorman, Ltd., 187 Westminster Bridge Road, S.E.

[2] Messrs. Davis Bros. make this mask and box. St. Thomas's Street, S.E.

pneumonia become strong and regular and has restored them to consciousness. On removal of the oxygen the patients return to their former state, to be temporarily restored again and again by oxygen. The indication seems to be that such patients should be kept continuously in a chamber containing say 50 per cent. of oxygen.

At high altitudes, such as Mexico City or Johannesburg, it is recognised that patients with pneumonia have the best chance if sent to the plains. If put continuously into a still higher partial pressure of oxygen than that at sea level pneumonic patients would probably do still better. The acid concentration of the blood would be lowered by such treatment in any other cases where there is oxygen want, *e. g.* cardiac cases. What is required is a chamber built on the plan of a gas-holder big enough to hold a patient and nurse, fitted with an air-lock, and containing a pan of caustic soda for absorbing the exhaled carbonic dioxide, and a cold-water coil for regulating the temperature.

Periodic or Cheyne-Stokes breathing is made regular by making the patient breathe either 3–4 per cent. CO_2 or oxygen. The respiratory centre is in such a state that it does not respond in the normal sensitive fashion to the acid concentration of the blood. When a concentration of acid is reached by lack of oxygen sufficient to excite it a period of breathing is set going. Carbonic acid is washed out of the body by this breathing, the concentration of acid falls, and the centre ceases to be excited until the concentration rises again, owing to lack of oxygen. The breathing of 4 per cent. CO_2 keeps the centre excited all the time; the breathing of oxygen on the other hand puts the centre into a better condition of nutrition so that it responds to the normal concentration of CO_2.

Just as in case of coal-gas poisoning so in case of poisoning by nitrites or nitro-compounds, such as nitro-benzene, oxygen must be administered. In this case the hæmoglobin is converted into methæmoglobin and is so made useless as a carrier of oxygen.

Many elderly patients who suffer from lesions of the heart, arteries and kidneys show considerable breathlessness but no cyanosis. Their breathlessness is not due to insufficient aeration or accumulation of CO_2, but to an acid intoxication of the blood. Just as in the case of the mountain sick, there is a retention of acids in excess of bases. These cases frequently show periodic breathing.[1]

Oxygen in high concentration acts as a poison. It produces inflammation of the lungs and causes convulsions. It would be risky to breathe continuously an atmosphere of oxygen for twenty-four hours. There is no risk in breathing oxygen for two to four hours, the time which miners inhale it who practise the use of breathing apparatus. There is not the slightest risk in administering oxygen to patients for brief intervals of time, in the way it is usually given. An atmosphere containing 50 per cent. of oxygen can be breathed indefinitely without harm.

Bernstein breathed oxygen at a pressure of two to three atmospheres—10–15 times the normal concentration. After an inhalation lasting forty-five minutes he experienced on one occasion slightly convulsive symptoms, but suffered no harm afterwards. The alarm expressed about the poisonous action of oxygen has been based on insufficient knowledge.

L. E. H.

[1] Lewis, Ryffel, Wolf, Cotton and Barcroft, *Heart*, Vol. V. p. 45, 1913.

APPENDIX

Summary of Principal Alterations in the British Pharmacopœia, 1914

By J. Langford Moore, F.C.S., M.P.S.

1.—NOTABLE ALTERATIONS IN POTENCY.

Stronger.

Acetum Scillæ .... 100 per cent.
Dose.—5–15 minims.

Acetum Urgineæ .... 100 per cent.
Dose.—5–15 minims.

Lin. Opii .... 33·3 per cent.

Spt. Juniperi .... 100 per cent.
Dose.—5–20 minims.

Syr. Chloral .... 9 per cent.
Dose.—½–2 fl. drs.

Syr. Codeinæ Phos. .... 9 per cent.
Dose.—½–2 fl. drs.

Tinct. Aconiti .... 100 per cent.
Dose.—2–5 minims.

Tinct. Camph. Co. .... 10 per cent.
Dose.—½–1 fl. dr.

Tinct. Opii .... 33·3 per cent.
Dose. {5–15 minims (repeated). 20–30 minims (single).

Tinct. Strophanth. .... 300 per cent.
Dose.—2–5 minims.

Ung. Hyd. Subchlor. .... 100 per cent.

Note.—The percentages in the above column indicate increases in strength, *e.g.* the strength of Acetum Scillæ is doubled and that of Tinct. Strophanthi quadrupled; the percentages in the adjoining column indicate decreases in strength.

Weaker.

Acid. Nitric. Dil. .... 42·7 per cent.
Dose.—5–20 minims.

Acid. Phosph. Dil. .... 27·5 per cent.
Dose.—5–20 minims.

Acid. Sulph. Dil. .... 26·7 per cent.
Dose.—5–20 minims.

Emp. Belladonnæ .... 50 per cent

Inj. Cocainæ Hypo. .... 50 per cent.
Dose.—5–10 minims (by injection).

Inj. Morphinæ Hypo. .... 50 per cent.
Dose.—5–10 minims (by injection).

Lin. Hydrargyri .... 40 per cent

Liq. Hydrarg. Per. .... 12·3 per cent
Dose.—½–1 fl. dr.

Liq. Potassæ .... 19·2 per cent.
Dose.—10–30 minims.

Pil. Phosphori .... 50 per cent.
Dose.—1–4 grains.

Syr. Ferri Iodidi .... 30 per cent.
Dose.—½–1 fl. dr.

Tab. Trinitrini .... 23 per cent.
Dose.—1 or 2 tablets.

Tinct. Belladonnæ .... 30 per cent.
Dose.—5–15 minims.

Tinct. Colchici .... 50 per cent.
Dose.—5–15 minims.

Tinct. Digitalis .... 20 per cent.
Dose.—5–15 minims.

Tinct. Nucis Vom. .... 50 per cent.
Dose.—5–15 minims.

Tinct. Opii Ammon. .... 10 per cent.
Dose.—½–1 fl. dr.

Troch. Acid. Carbol. .... 50 per cent.

Ung. Acid. Carbol. .... 25 per cent.

Ung. Hydrargyri .... 38 per cent.

Ung. Hydrarg. Amm. .... 50 per cent.

Ung. Hydrarg. Co. .... 38 per cent.

2.—NOTABLE ALTERATIONS IN NOMENCLATURE.

Old Name (1898).		New Name (1914).
Acet. Cantharidis	=	Acet. Cantharidini
Emp. Cantharidis	=	Emp. Cantharidini
Ext. Aloes Barb.	=	Ext. Aloes
Ext. Bellad. Alch.	=	Ext. Bellad. Siccum
Ext. Cascaræ Sag.	=	Ext. Cascaræ Sag. Siccum
Ext. Euonymi Siccum	=	Ext. Euonymi
Ext. Hyoscyami Viride	=	Ext. Hyoscyami
Ext. Nucis Vom.	=	Ext. Nucis Vom. Siccum
Ext. Opii	=	Ext. Opii Siccum
Ext. Viburni Prun. Liq.	=	Ext. Viburni Liq.
Ferrum Tartaratum	=	Ferri et Potassii Tartras
Ferri Phosphas	=	Ferri Phosphas Saccharatus
Hydrargyri Oleas	=	Hydrargyrum Oleatum
Liq. Iodi Fort.	=	Tinct. Iodi Fort.
Liq. Magnes. Carb.	=	Liq. Magnes. Bicarb.
Oleum Gynocardiæ	=	Oleum Chaulmoogræ
Oleum Pini	=	Oleum Abietis
Pil. Aloes Barb.	=	Pil. Aloes
Pil. Aloes Soc.	=	Pil. Aloes
Syr. Codeinæ	=	Syr. Codeinæ Phos.
Tinct. Colch. Sem.	=	Tinct. Colchici
Tinct. Iodi	=	Tinct. Iodi Mitis
Troch. Eucalypti Gummi	=	Troch. Kino Eucalypti
Ung. Cantharidis	=	Ung. Cantharidini
Ung. Glyc. Plumbi Subacet.	=	Ung. Plumbi Subacet.
Ung. Gynocardiæ	=	Ung. Chaulmoogræ

3.—NOTABLE ADDITIONS—ORGANIC CHEMICALS.

B.P. Name.	Other Names.
Acetylsalicylic Acid	Aspirin; Helicon; Xaxa
Adrenalin	Adrenine; Suprarenin
Barbitone	Malourea; Veronal
Benzamine Lactate	Betacaine or β-Eucaine Lactate
Chloral Formamide	Chloramide; Chloralamide
Diamorphine Hydrochloride	Acetomorphine; Heroin
Formaldehyde Solution..............	Formalin; Formol
Hexamine	Formamine; Urotropine
Methylsulphonal....................	Sulphonethylmethane; Trional
Phenolphthalein	Laxoin; Phenolax; Purgen
Resorcin	Resorcinol
Theobromine and Sodium Salicyl	Diuretin; Theobromine Sodio-salicylate

Inj. Strychninæ Hypod. ·75 per cent.
Dose.—5–10 minims.

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